IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF SOUTH CAROLINA

CHARLESTON DIVISION

- - -

CERTIFIED COPY

SUZANNE Q. LITTLE, individually and as Personal Representative of the Estate of SAMUEL MARTIN LITTLE, Deceased,

Plaintiff,

vs.

No. 2-98-1879-23

BROWN & WILLIAMSON TOBACCO CORPORATION, individually and as successor by merger to THE AMERICAN TOBACCO COMPANY, and R.J. REYNOLDS TOBACCO COMPANY,

Defendants.

DEPOSITION OF

SAMUEL P. HAMMAR, M.D.

SEATTLE, WASHINGTON

APRIL 10, 2000

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Defendants.	)	

Deposition of SAMUEL P. HAMMAR, M.D., taken on behalf of Defendants, at the Four Seasons, 114 University, Seattle, Washington, commencing at 8:00 a.m., Monday, April 10, 2000 before Suellen H. Shaw, CCR No. SHAW*SH565PS.

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(None)

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(Defendants' Exhibit 1 was marked for identification.)

SAMUEL P. HAMMAR, M.D.

having first been duly sworn, was

examined and testified as follows:

EXAMINATION

BY MR. MURPHY:

Q. Dr. Hammar, good morning.

A. Good morning.

Q. We introduced ourselves off the record, but let me do it on the record. My name is Dennis Murphy, and I'm here today representing R.J. Reynolds Tobacco Company. Okay?

A. All right.

Q. I know you have been through this process, that is a deposition, on several prior occasions. Is that correct?

A. Yes.

Q. You're familiar with this process?

A. Yes.

Q. Be that as it may, let me tell you that today I'm going to ask you a series of questions.

A. Yes.

Q. If my questions call for a yes or no answer, can you try and limit your answer to a yes or no?

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A. Yes.

Q. If my questions call for a more discursive answer, will you try to provide that?

A. Yes.

Q. As we go along today, if you don't hear my questions, would you let me know that so I could repeat them?

A. Yes.

Q. If there is ever a question that you don't understand, would you let me know that as well?

A. Yes.

Q. I am not a doctor and certainly not a pathologist. From time to time today I might use terms incorrectly, or more likely I might mispronounce terms. If I do that would you help me out?

A. I certainly will. I'll be very forgiving.

Q. I know we are going to talk a little bit about some staining, and my first-time pronunciations, I'm sure, are going to be a little off.

A. No problem.

Q. Let's talk a little bit about your experience as an expert witness in litigation, okay?

A. Sure.

Q. I've reviewed some of your prior testimony and, as I understand it, at some point last year you had --

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at that point in time you had testified in approximately 75 trials?

A. Approximately, yes.

Q. Is that the number you'd use today, or would it be a little bit more?

A. A little bit more.

Q. Somewhere in the neighborhood of 80 trials you've testified in?

A. Approximately, yes.

Q. Is there a better number you can give me as we sit here?

A. Not any better than that.

Q. In addition to that testimony at trial, as we said in the beginning, you have been deposed numerous times; is that right?

A. Yes.

Q. I know I had some testimony from 1995 where at that point in time you had been deposed in at least 300 cases?

A. I believe that's correct.

Q. Do you have a number, as of today, in terms of the amount of times you have been deposed?

A. I'd say 375. The number of depositions has slightly decreased lately.

Q. You think it's only 75 depositions since '95?

http://legacy.library.ucsf.edu/tid/rax00/pdf Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

A. I believe so, yes.

Q. In the past you've testified that you've reviewed over 7,000 cases for litigation; does that sound accurate?

A. It does, yes.

Q. Is there any way you can bring that number up to date? Is that still accurate, over 7,000?

A. That's approximately correct. That's an approximate number, yes.

Q. Now, in the past, also, you testified that 99 percent of your litigation work was in asbestos cases?

A. Yes.

Q. Does that remain true?

A. Yes.

Q. In the past, also, you've said that 99 percent of your litigation work was for plaintiffs?

A. In the last ten years that's true, yes.

Q. That remains true to this date for the last ten years?

A. Yes.

Q. Now, despite that the great majority of your litigation work has been in asbestos cases, you have been involved in several tobacco cases more recently?

A. Yes.

Q. In the last year, right? I guess I should say

http://legacy.library.ucsf.edu/tid/xaa00f00 Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

in 1999, which was the last year, you testified in four tobacco trials; is that correct?

A. I believe that is correct, yes.

Q. You testified in the Henley trial?

A. Yes.

Q. In the Williams trial?

A. Yes.

Q. In the Butler trial?

A. Yes.

Q. And in the Gilboy trial?

A. Yes.

Q. Were there other tobacco trials that you testified in last year?

A. The only other tobacco trials would have dealt with Kent cigarettes micronite filters and asbestos but not tobacco, per se.

Q. How many of those trials have you testified in?

A. About five.

Q. So if I were to ask for a number of times you testified for plaintiffs at trial against the tobacco industry, it would be nine times?

A. If you count the asbestos and micronite Kent cases, yes.

Q. And I probably should have asked this question

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

before the last one. All of your testimony at trial in tobacco litigation has been for the plaintiffs?

A. It has. The Kent cases, of course, are different than the four cases that you mentioned in that they are not dealing with the disease lung cancer but dealing with the disease mesothelioma which is not related to carcinogens present in tobacco smoke but are related to asbestos present in the micronite filters that were present in Kent cigarettes between 1952 and 1956.

Q. What I'm getting at is both of those kinds of cases you testified for the plaintiffs?

A. Yes.

Q. Aside from the cases that you've testified in, you've also been deposed in other tobacco cases?

A. Yes.

Q. I know you were deposed in the Whiteley case?

A. I was.

Q. Were there other cases aside from Whiteley that you have been deposed in?

A. That's what I was just trying to think of. I think there was one other or maybe two others, but I cannot remember their names.

Q. Were they within the last year or further back?

A. I think they were further back. I remember

http://legacy.library.ucsf.edu/tobacco/pdf/www.industrydocuments.ucsf.edu/docs/tgxl0001

one. One was actually for Jerry Covert (phonetic). Actually there were two cases for Jerry Covert: one, the Gilboy case --

Q. Was the other the case brought by his wife or on behalf of his wife?

A. Right. That's correct, yes.

Q. Is there another case besides that one?

A. I think there is one other cases, but I cannot remember the name.

Q. Was that for Mr. Covert, again?

A. No, it was not for Mr. Covert. It was for someone else.

Q. Aside from the cases that we've mentioned so far and aside from this case, the Little case, are you working on other tobacco cases currently?

A. No. The only other thing -- now I remember. The only other ones that I reviewed and did work in and gave a deposition in were the Farnan case and the Della Vecchia case that were in Florida, and I think the trials were completed.

Q. That was part of the Engle class action; is that what that was called?

A. Yes.

Q. Now, the one case that we mentioned you testified in was the Butler case?

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A. That was one of them. I've testified in three tobacco cases -- actually four: the Butler case, the Gilboy case, the Williams case, and the Patricia Henley case.

Q. Let's talk about Butler for a minute, okay?

A. Okay.

Q. Your initial involvement in the Butler case was through the Ness, Motley firm; is that right?

A. Yes.

Q. The Ness, Motley firm, they are the firm that represents the plaintiffs in this case, the Little case?

A. Yes.

Q. You also were involved in several asbestos cases with the Ness, Motley firm; is that right?

A. Yes.

Q. Can you give me any estimate of the number of cases you have been involved with the Ness, Motley firm?

A. I would say over the years probably 75 to 100 cases. That's an estimate.

Q. Most of those have been asbestos cases?

A. They all have been asbestos cases.

Q. Outside of this case and the Butler case?

A. Right.

Q. Now, have you ever been asked to become involved in a tobacco case in which you then declined to become involved?

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A. Not that I can think of, no.

Q. Let me try another question that's a little bit different.

Have you ever reviewed materials in a tobacco case that was in litigation and came to the conclusion that you could not determine that the injury involved was caused by cigarette smoking?

A. I have reviewed cases in which both asbestos and tobacco have been an issue in a lung cancer case where I have concluded that I could not determine if tobacco was the cause of the lung cancer.

Q. Were those cases that were brought against asbestos companies or tobacco companies to your knowledge?

A. Asbestos companies.

Q. In those cases you concluded that it was the asbestos and not the tobacco smoking that caused the disease at issue?

A. Well, it was something like that, or more likely that I could not determine if tobacco was a factor causing the lung cancer, usually because the number of pack years of smoking was relatively small and the time since the person last smoked was many years prior to the diagnosis of lung cancer.

Q. Now, obviously, you charge for your time in litigation?

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A. My laboratory charges for our time, yes -- my time.

Q. What are your current litigation charges?

A. Current litigation charges are $350 an hour for deposition testimony, $350 an hour for trial testimony, $250 an hour to review medical records and pathology materials, $200 for time away from the office with a maximum of a 12-hour day.

Q. So your maximum daily charge is $2,400?

A. That's correct. And if I participated in a trial during that day, I would subtract the number of hours that I testified at trial from that 12 hours and that would be the amount our laboratory would charge for my time away from the office.

Q. You say it's what your laboratory charges, but you're an owner of the laboratory?

A. I am a quarter owner of our laboratory. I have three other partners. All the profits that are made from my work doing this are split equally between myself and my three partners.

Q. I think it was at the Butler trial that you testified that approximately 50 percent of your professional time was spent on litigation matters?

A. That's correct. Primarily asbestos cases, yes.

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

Q. Does that remain true today that approximately 50 percent of your time is spent on litigation?

A. It does, yes.

Q. Now, from what I gleaned from reviewing some testimony is that the percentage of time you spend on litigation has increased since 1995 when you were deposed in the Gilboy case; is that fair to say?

A. It has. The last three to four years it has increased, yes.

Q. Back in '95 at the Gilboy deposition you testified that 50 percent of your income was from litigation activities; do you recall that?

A. I don't recall that because that's probably not true. I don't know maybe how the question was stated, but that's not true.

Q. My question was going to be: If your income was 50 percent from litigation at that point in time and the time you spend on litigation has increased, is your income currently more than 50 percent from litigation?

A. No. It's less than 50 percent. As I said, any profits that our laboratory made are split equally between myself and my three partners.

Q. What would be your estimate of the income you received from litigation activities today?

A. Me personally in a year?

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

Q. Yes.

A. In the neighborhood of 75 to $80,000.

Q. I'm sorry. I was looking for a percentage of your income?

A. Oh, a percentage. I can't give you that percentage. I don't know exactly what it is. I'm not at will to do that according to the rules of our partnership -- our corporation. I can give you what I personally make, and that's what I told you. The number I gave you is what I personally make a year, at this point in time, from litigation.

Q. As you sit here today, you are not going to tell me what percentage that is of your total compensation?

A. No. The by-laws of our agreement with my partners prohibit me from doing that.

Q. When were you first contacted about becoming involved in the Little case?

A. It was initially contacted by phone call from Mr. Charles Patrick of the Ness, Motley law firm. It would have been, I'd say, a couple of days prior to February 17, 2000.

(Defendants' Exhibit 2 was marked for identification.)

Q. BY MR. MURPHY: I want to hand you what we have had marked as Exhibit 2 to your deposition today and ask you to take a look at that and tell me if you have seen

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

that letter.

MR. MURPHY: I have copies of most of this stuff. I might forget to hand them over, so just gently remind me if you need a copy.

A. (Perusing.)

Q. BY MR. MURPHY: Doctor, I notice you are flipping through some materials you have brought with you today.

A. Yes.

Q. Is that your file in this case?

A. Yes.

Q. And you are looking to see if you have a copy of the letter marked as Exhibit 2?

A. I don't, and I don't recall seeing this.

Q. For the record, Exhibit 2 is a letter dated March 10, 2000, from Charles Patrick to A.J. Singleton; is that correct?

A. It is.

Q. My only question about Exhibit 2, this letter, comes from the first line of it where Mr. Patrick is suggesting that "Our expert pathologist, Dr. Russell Harley, suggested that we have immunohistochemical stains performed to provide additional information as to the cell type of Martin Little's lung cancer. He stated that he did not have the appropriate materials for the necessary

http://legacy.library.ucsf.edu/tid/xaa00h00/pdf Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

immunohistochemical stains readily available in his laboratory, and he suggested that we should send the pathology slides and blocks to Dr. Hammar for immunostaining."

Do you see that?

A. I do.

Q. Did you have an understanding that the suggestion to get you involved in this litigation came from Dr. Harley?

A. Yes.

Q. Is that what Mr. Patrick told you during his initial conversation with you?

A. As I recall, yes.

Q. Now, you know Dr. Harley; is that right?

A. That's right.

Q. Do you know him professionally?

A. Yes.

Q. Do you know him personally as well?

A. A little bit, yes.

Q. Dr. Harley wrote one of the chapters in your book?

A. He did.

Q. By the way, I have your book here. I think it's the second edition. Is there a new edition coming out in the near future?

http://legacy.library.ucsf.edu/tid/fas00b00/pdf Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

A. Maybe. I can't say for certain. It depends on several things.

Q. Is a new edition in the works?

A. A new edition has been asked for by the publisher. We have given them the table of contents. The way medicine has changed in the last few years, it's very hard for people to have time to do much writing anymore.

Q. Is it that you are not sure whether you will put out a new edition or that you are not sure when a new edition will come out?

A. I little bit of both.

Q. Now, in the second edition of your book -- and it's Dail and Hammar Pulmonary Pathology, Dr. Harley wrote the chapter dealing with tobacco; is that right?

A. Yes.

Q. Has there been any determination of who would write the chapter on tobacco for any possible forthcoming third edition?

A. There has been some talk about that. Personally, I wanted Dr. Harley to do the chapter again. Dr. Dail, who was my coeditor, thought that maybe he would try to get somebody else. One name that was possibly suggested was Dr. Douglas Henderson who is a pathology in south Australia.

Q. Have any other names been mentioned to do the

http://legacy.library.ucsf.edu/tid/ras00f00 Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

chapter on tobacco in your possible third edition?

A. Not that I can recall, no.

Q. Do you know a pulmonologist by the name of Allen Feingold?

A. I do.

Q. Have you contacted Dr. Feingold about writing any chapters in a possible forthcoming edition of your book?

A. I have not, but Dr. Dail may have. I don't know.

Q. As far as you know, though, are there no plans for Dr. Feingold to write a chapter?

A. I wouldn't say there are any plans, but I mean --

Q. I'm trying to qualify that by saying "as far as you know."

A. As far as I know, but I don't know if we discussed that that thoroughly.

Q. Now, Dr. Harley suggested that the pathology be sent to you for staining?

A. He did.

Q. Does Dr. Harley have a lab that can do this type of staining?

A. He has a lab that I'm sure can and does immunohistochemical tests. The specific tests that he wanted is a problem because there is no commercial antibody

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

available against the test that he wanted done. He thought I may have had that antibody, which I did not; but I have a good friend here in Seattle who did have that antibody.

Q. And that's Dr. Allen Gown who had the antibody?

A. That's correct.

Q. To your knowledge would Dr. Harley have had the proper materials, the proper stains, to do the staining that you did in your lab?

A. That I really don't know.

Q. But he likely didn't have the stain that Dr. Gown used?

A. I don't think he did because for some reason that antibody is only commercially available in Japan even though it's produced by a company who is well known in the United States. It's not available in the United States commercially.

Q. In your work as a pathologist, you review pathology outside of the litigation context?

A. Sure.

Q. Has Dr. Harley ever sent you pathology to review or stain outside of the litigation context?

A. Yes.

Q. Can you give me an approximate number of times when he has done that?

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A. The only time I can remember is one time, and that had to do with a case of interstitial fibrosis of the lungs in which there were a lot of eosinophils, and Dr. Harley wanted to know if the presence of eosinophils imposed a poor prognosis on a person who had interstitial fibrosis. I reviewed the case and sent him some literature concerning eosinophils and their potential significance in interstitial pulmonary fibrosis.

Q. I want to back up a minute and make sure I asked the right question.

Was this a case that as far as you know was not a case in litigation; it was a case that Dr. Harley was reviewing for treatment of a patient?

A. Yes.

Q. In the litigation context, has Dr. Harley sent pathology to you for review and/or staining?

A. I don't recall any other cases that he sent to me for staining. I think there have been other cases where the Ness, Motley law firm has had Dr. Harley review the case and I have also reviewed the case; but I don't believe, to the best of my knowledge, that there have been any other cases where he has sent me material for immunohistochemical staining.

Q. If I understand this correctly, you sent some of the pathology on to Dr. Gown's lab because you didn't

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

have that stain available; is that right?

A. Yes. What we did is we cut tissue sections from the blocks that are designated in my report and sent those slides that were put on a special type of glass slides for immunohistochemical staining to Dr. Gown's laboratory where a surfactant ApoA1 stain was done.

Q. Would Dr. Gown's laboratory have been able to do the staining that you did in your lab?

A. Yes.

Q. I want to step back a minute to that initial phone call you received from Mr. Patrick regarding the Little case. What did you and Mr. Patrick discuss in that call?

A. It's been a while, and I can't tell you everything that we discussed. What I remember is that he told me this was a case that Dr. Harley had reviewed and that it was a case of a lung cancer in a person who was a cigarette smoker. He stated that there was a statement by an individual who had reviewed the case for you folks who stated that this tumor was a bronchioloalveolar cell carcinoma and that Dr. Harley wanted to have stains done for a substance that would commonly be seen in that type of lung cancer, specifically surfactant apoprotein.

Q. So Mr. Patrick is the one who told you that Dr. Harley thought that a surfactant apoprotein stain should

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

be done?

A. As I recall, yes.

Q. Did Mr. Patrick at any time suggest to you other staining that should be done?

A. No.

Q. So the other staining you did -- well, let me ask it more as a question.

Did anyone else suggest to you the other staining that you did?

A. No.

Q. It was your decision to do those stains?

A. It was my decision based on the histological appearance of the tumor, yes.

Q. I take it from your answer that Mr. Patrick told you that Dr. Harley was involved in this case?

A. Yes.

Q. And that he had reviewed the pathology?

A. Yes.

Q. Did Mr. Patrick tell you about any other pathologist involved in the case for the plaintiffs?

A. Yes.

Q. Who did he tell you about?

A. Dr. Victor Roggli, R-o-g-g-l-i.

Q. Now, you also know Dr. Roggli?

A. Very well.

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

Q. You know him professionally?
A. Yes.
Q. And you also know him personally?
A. One of my best friends.
Q. Dr. Roggli has also contributed chapters to your textbook?
A. He has. Chapter 27.
Q. Do you know if Dr. Roggli has a lab capable of doing immunohistochemical staining? Let me first ask you to limit your answer to the staining of the type that you did.
A. In general, yes; but I don't know specifically if he has all of the same antibodies that we have, although I'm pretty sure that he does.
Q. Do you know if Dr. Roggli would have the necessary materials to do the staining that you had Dr. Gown's lab do?
A. I'm quite sure that he would not.
Q. Did Mr. Patrick, during this initial phone call, tell you what Dr. Harley or Dr. Roggli had diagnosed the cancer cell type as?
A. I don't remember.
Q. Now, after Mr. Patrick told you that he would like -- through Dr. Harley that he would like to have the pathology stain for surfactant apoprotein, did you tell him you could not do that at your lab?

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

A. I told him that that antibody was not commercially available and that we did not have it. I told him I had a good friend in Seattle who had an immunohistochemistry laboratory who could do that.

Q. Did Mr. Patrick approve of you sending pathology over to Dr. Gown's lab for staining?

A. As I recall, yes.

Q. In your words could you describe what you viewed as your role in this case after your conversation with Mr. Patrick?

A. I viewed my role as a person who was going to review this case and primarily to facilitate the testing of the tumors in Mr. Little's lungs for the surfactant apoprotein. I think that the case has been thoroughly reviewed by Dr. Harley and Dr. Roggli and that I probably add relatively little to anything that they had already, but I think that I was the person that could get the surfactant apoprotein tests performed which was something that Dr. Harley thought would be useful.

Q. That's the test that was ultimately performed by Dr. Gown's lab?

A. That's correct, yes.

Q. I haven't handed it to you yet, but we have marked as Exhibit 1 the notice of your deposition.

A. Yes.

http://legacy.library.ucsf.edu/tid/fas00/pdf Source: http://www.industrydocuments.ucsf.edu/docs/tgxl0001

Q. And I'll give you a copy of it so you can take a look at it.

A. All right.

Q. You received a copy of Exhibit 1?

A. Yes.

Q. And that asked you to bring certain materials with you today?

A. Yes.

Q. I think I mentioned on the record before that you brought your file in this case; is that right?

A. Yes.

Q. Did you bring your whole file?

A. Yes.

Q. You just brought the original; you didn't bring copies?

A. I did not bring copies.

Q. Maybe at a break we can take a look at what you have brought with you today, but you bought that in response to the deposition notice?

A. Yes.

Q. You've also brought at least a textbook and some other pamphlets or photocopies. What are they?

A. I brought the current WHO book on the classification of lung and pleural tumors. I brought the book that I'm a co-editor of called Pulmonary Pathology

http://legacy.library.ucsf.edu/tid/rax00/pdf Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

Tumors which has a chapter in it that is basically the same as Chapter 32 in that larger book. I brought the initial WHO Histologic Typing of Lung Tumors. I brought a copy of the second Histologic Typing of Lung Tumors.

Q. Is it fair to say that contained in your file is all the written or documentary information you have on the Little case?

A. Yes.

Q. I want to talk about the materials you received in the Little case in general; and I'll tell you as we start, let's leave pathology to the side and we can do that at the end.

A. Okay.

Q. Did you receive any of the radiology for Mr. Little?

A. I don't quite understand what you mean by that. Do you mean actual x-rays, or do you mean radiology reports?

Q. Let's start with actual x-rays or CT scans. Did you receive any of those?

A. No.

Q. Did you receive any x-ray reports or CT reports?

A. No.

Q. In terms of the medical records of Mr. Little,

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looking at your file, I think it's fair to say that you did not receive a complete set of Mr. Little's medical records; is that correct?

A. Yes.

Q. What medical records from Mr. Little did you receive?

A. (Perusing.) I received a hospital discharge summary from the Medical University of South Carolina. That discharge summary stated that Mr. Little was admitted on March 31, 1999 and discharged on April 9, 1999. The report was by Lawrence B. Afrin, A-f-r-i-n, M.D., attending.

I actually misspoke previously. I did receive a CT scan of the chest on Mr. Little, a report that was by Lynn Coppage, C-o-p-p-a-g-e, and this is dated April 1, 1999. That is the only report that I received from the treating facility.

Q. Am I correct that you received those --

A. Excuse me. I'm making a mistake. I also received a surgical pathology report.

Q. I don't want to get ahead of you and I'm happy to hear it now, but we were going to try to leave pathology to the side. I'm most happy for you to explain that you did receive --

A. No.

Q. Let's make it clear. You did receive certain

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medical records relating to the pathology that was reviewed on Mr. Little?

A. Yes.

Q. Let's put those to the side for a minute until we get to pathology.

I take it that any of the medical records you received in this case you received through the plaintiff's attorneys; is that right?

A. Yes.

Q. Do you know why they sent you the hospital discharge report that you referenced?

A. I think that's a reasonable thing to send a pathologist like myself who is going to review the pathology materials because that gives an overview of the case and often what happened to a patient, at least as part of their medical care. It generally would not be necessary to send a person like myself all of the medical records especially after Dr. Harley and Dr. Roggli had both reviewed this case.

Q. I'm trying to break down your answer and get an understanding of what you might be saying.

Is it fair to say that it's your thought that that record was sent to you not necessarily because of the specific reasons that Mr. Little was hospitalized during those times referenced in the record but because the record presents a general overview of Mr. Little's medical history?

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A. I believe that is correct, yes.

Q. What is your understanding of why the plaintiff's attorney sent the record of the CT chest scan from April 1, 1999?

A. Again, I think that's just additional information which provides some insight into what type of abnormalities were found in his lungs.

Q. Again, it wasn't necessarily for the purpose of any findings that were specific to April 1, 1999?

A. I think it was just given as an overview as to what was happening to Mr. Little, but that information was also provided in Dr. Harley, report, which I read.

Q. It's fair to say from what we've talked about so far that you haven't been given any depositions that have been taken in this case; is that correct?

A. Yes.

Q. For example, you haven't been given the depositions that were taken of Mr. Little or of his wife; is that correct?

A. Correct.

Q. You haven't been given any deposition transcripts that were taken of the other experts in this case; is that right?

A. Yes.

Q. We'll get to it in a little more detail later

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on, but one of the other experts that you mentioned in one of your letters or your report was a Dr. David Burns; do you recall that?

A. (Perusing.) I do recollect that, yes.

Q. Doctor, it might be helpful, since we are going to talk about these at least in some detail over the course of the day -- two further additions.

MR. MURPHY: Let's mark this as 3 and this as 4.

(Defendants' Exhibits 3 & 4 marked for identification.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you what I've had marked as Exhibit 3 to your deposition and ask you to take a look at that.

A. Okay.

MR. EVANS: May I have a copy of the exhibit?

MR. MURPHY: Sure.

Q. BY MR. MURPHY: Doctor, do you recognize Exhibit 3?

A. I do.

Q. That's a letter from you to Mr. Charles Patrick at the Ness, Motley firm dated March 8, 2000?

A. Yes.

Q. To summarize it generally, this is a letter you sent along with your expert report to Mr. Patrick on that date; is that fair?

A. Yes.

Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

Q. Let me now show you what we've marked as Exhibit 4.

A. (Perusing.)

Q. Doctor, do you recognize Exhibit 4?

A. Yes.

Q. That's a copy of your report in this case; is that correct?

A. Yes.

Q. Now, I had mentioned Dr. Burns, and you see that on the first page of Exhibit 4 of the report that you referenced Dr. Burns there; is that right?

A. Yes.

Q. Do you know Dr. Burns professionally or by reputation?

A. No.

Q. Have you ever collaborated with him in any way outside of the litigation context?

A. No.

Q. To your knowledge have you ever been involved with litigation with Dr. Burns before?

A. I don't know.

Q. That's fair.

Have you ever met Mr. Little or his wife?

A. No.

Q. Have you ever had conversations with them?

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A. No.

Q. Have you ever -- let me strike that.

As you were going through your file, I think you referenced then or in a prior answer expert reports that you had received from the plaintiff's attorney?

A. Yes.

Q. I know you received Dr. Harley's report.

A. Yes.

Q. Did you also receive Dr. Roggli's report?

A. Yes.

Q. Did you receive reports from any of the other experts in the case?

A. No.

MR. MURPHY: Just as a matter of housekeeping because we might refer to them from time to time, let's go ahead and mark a copy Dr. Harley's report as Exhibit 5 and Dr. Roggli's report as Exhibit 6.

(Defendants' Exhibits 5 & 6 marked for identification.)

Q. BY MR. MURPHY: Doctor, let me hand these to you and ask you if those are copies of the reports you received prepared by Drs. Harley and Roggli?

A. (Perusing.) Yes.

Q. Now, in one of your answers -- I think it was about the conversation you had with Mr. Patrick -- you mentioned a pathologist who was working as a defense expert

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in the case; do you recall that?

A. Yes.

Q. Did Mr. Patrick identify who that pathologist was?

A. I don't remember.

Q. Am I correct that you did not receive a report from that pathologist?

A. You are correct, yes.

Q. In fact, you haven't received reports from any of defendants' experts in this case?

A. That Is correct.

Q. Have you had any conversations with any of the plaintiff's experts in this case about the Little case?

A. No.

Q. You haven't talked with Dr. Harley about the Little case?

A. No. I talked to Dr. Harley recently at the United States and Canadian Academy of Pathology meetings but did not talk about this case.

Q. You haven't talked to Dr. Roggli about the Little case?

A. No.

Q. The meeting you mentioned was it with Dr. Harley -- or your conversations with Dr. Harley, were they at the meeting in New Orleans?

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A. Yes.

Q. Dr. Roggli was also at that meeting; am I right?

A. Yes.

Q. Did speak with Dr. Roggli in New Orleans?

A. Yes.

Q. But you did not speak about the Little case?

A. No.

Q. Correct?

A. Correct. I did not speak about the Little case.

Q. Doctor, we were provided with a copy of your CV which I'll have marked in the record.

I guess before I do that, do you know if you have a more current copy than the one we were provided with?

A. I think that's the most current. There are several things that are not on there that need to be put on there, but it seems like there's not enough time to do that. I don't think there's anything that relates to this case.

MR. MURPHY: Let's go ahead and mark this as Exhibit 7.

(Defendants' Exhibit 7 was marked for identification.)

Q. BY MR. MURPHY: Now, Doctor, I've placed before you a copy of the CV that we received which we've marked as Exhibit 7.

Source: https://www.industrydocuments.ucsf.edu/docs/fgxl0001

Before we went off the record for a minute, you started to say that there are some things not on there that probably should be included; is that right?

A. Yes. There are several other articles that I am either the first author or co-author on that are not there, and there's a couple of chapters in books that I've written that are not on there. I don't think any of them directly relate to this case.

Q. As far as you know -- and I think we said this -- this is the most up-to-date CV that you have?

A. I believe it is, yes.

Q. The one thing I wanted to ask you about your CV is under "Positions Held" and the first entry there?

MR. MURPHY: Do you need a copy, Jerry?

MR. EVANS: Yes.

Q. BY MR. MURPHY: It notes that you were on the panel for reclassification of lung tumors, World Health Organization, 1995 to the present?

A. Correct.

Q. What was your role on the panel for the reclassification of lung tumors of the WHO?

A. To produce this document which has been produced -- this book.

Q. When you said "this book," you are talking about Histological Typing of Lung and pleural Tumors,

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third edition, by the WHO; is that right?

A. Yes.

Q. How did your involvement on that panel lead to the production of that book?

A. I think I did just as much work as anybody who is listed on this first page or any other page. We basically all did a lot of work, which was going through a large number of cases discussing how certain types of neoplasms of the lung and pleura should be classified, showing examples of such neoplasms, reviewing slides in a blinded way and determining how accurately we agreed on certain classifications, and a very thorough and very long discussion of neoplasms of the lung and pleura which ended up in this book.

Q. Are there areas or parts of the book that came out that you weren't involved in?

A. No. I was involved in everything that's in this book with respect to what is written. There were several drafts of this book that we all went through, and we all had our input. I think everything that's in this book I contributed to.

Q. Do you stand behind what's in that book?

A. Sure.

Q. Similarly; do you stand behind what's in your text, Dail and Hammar Pulmonary Pathology, second

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edition?

A. Yes.

Q. Now, when we talked about the materials that you had received regarding this case from the plaintiff -- before we get there, I noticed when you held up the WHO book that you looked at some of the names listed either on the cover or on the first few pages. Is your name listed in the book?

A. It is. It's on page Roman numeral seven.

Q. Was there a reason for the distinction between those listed on the cover and those not listed until inside the book?

A. I don't know exactly how it was decided whose name should be put on there first. I would say Bill Travis and Tom Colby and Dr. Shimosato were the primary people who I think provided probably the greatest input to the book; although, everybody worked very hard on this book.

I don't think Dr. Corrin or Dr. Brambilla, for example, worked any harder than I did or anybody else of the core members; but it doesn't really make much difference to me one way or another. I think what makes a difference is that the quality of this came out what I would consider excellent, and that's the most important thing.

Q. A portion of information that we had left to the side when we talked about what you received from

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plaintiff's attorneys regarding the Little case was pathology. Let's start, I guess, with the copies of the records of the pathology reports that you received from the plaintiff's attorneys.

A. (Perusing.)

Q. Can you list those for me?

A. Sure. The first one has a pathology number of SP-95-20474-9550005, and the accession date on that is December 18, 1995.

The pathology report indicated that it consisted of two parts. Part A was a biopsy of a left upper lobe lesion, and Part B was an anterior mediastinal node.

Q. That's enough for now. What's the next report?

A. The next one is SP-96-04435-9550005, accession date of March 11, 1996. That was the resected left upper lobe and nymph nodes. That case consisted of six parts.

The last is designated as SP-96-16688-9550005, accession date of September 17, 1996. That was a biopsy of a right lower lobe lesion.

Q. Those are the three pathology reports for Mr. Little that you received from plaintiff's attorneys?

A. Yes.

Q. Am I correct, now, that we have gone through and listed all the medical records you received from

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plaintiff's attorneys?

A. Yes.

Q. Now, let's change gears a little bit and talk about the pathology that was actually sent to you.

A. All right.

Q. I guess to do that maybe the easiest thing to do is to refer to your report which we have marked as 4, I believe.

A. Yes.

Q. You probably have another copy of that in your file. Is it easier for you to use your copy?

A. I'll use my copy if that's okay.

Q. You don't have any notes or anything else on your copy, do you?

A. No.

Q. That's fine if you use your copy. I think your report does it at the top, but let's try to list the pathology materials you received from the plaintiff's attorneys. Can you go ahead and do that for me?

A. Sure. I received 17 glass slides and 16 paraffin blocks that were designated SP96-4435. I received two glass slides and three paraffin blocks designated 96-16688.

Q. That's the sum total of the pathology material you received from plaintiff's attorneys?

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MR. MURPHY: Yes. At the risk of putting a lot of things out there before us early, I'm going to go ahead and ask that copies of the three pathology reports you received be marked so that if we need to refer to those we can.

(Defendants' Exhibits 8 - 10 marked for identification.)

Q. BY MR. MURPHY: Doctor, let me hand you copies of what we've marked as Exhibits 8, 9 and 10 to your deposition and ask you if those are copies of the pathology reports you received from plaintiff's counsel?

A. They are not exactly the same, but they have the same information in them. I don't know why they are not exactly the same, but it doesn't make much difference.

Q. Okay. Because those are copies of the records we had collected from the hospitals -- and I know that -- I might use the ones that we marked as exhibits when we can, and maybe we'll make an effort to get copies of what you have at some point in time during the course of the day so we can deal with that if the exhibit needs to be dealt with.

Is it fair to say, though, that you received two sets of pathology that match up to two of those reports -- two of the three reports?

A. Yes.

Q. You received a set of pathology's 17 slides and 16 blocks labeled SP-96-4435, and they match up to the pathology report that's been marked as Exhibit 9; is that

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right?

A. Yes.

Q. Then you received two slides and three blocks labeled 96-16688, and they match up to the report that's been marked as Exhibit 10; is that right?

A. Yes.

Q. You did not receive pathology that would match up with the pathology report that we've marked as Exhibit 8; is that correct?

A. Yes.

Q. Do you know why you never received such pathology?

A. Not specifically, no.

Q. Did you ever ask Mr. Patrick or any of the other plaintiff's lawyers why it was that that pathology was not sent to you?

A. I did not. I knew of this report, and I didn't consider it critical that I review this because this represented only the additional biopsy that documented the cancer.

Q. If you were diagnosing a patient outside of the litigation setting, in the hospital setting, regarding whether they had lung cancer and, if so, the cell type of the lung cancer that they had, would you want to review all of the pathology that existed on that patient?

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A. In general, yes.

Q. One thing I wanted to ask you about was -- again, I guess we can look at your report for the numbers, but your listing that there were 17 slides from SP96-4435 and two slides that matched up with 96-16688, do you see that?

A. I do.

Q. Did you notice that one of those slides was really mislabeled so that there were 16 slides from SP96-4435 and three from 96-16688?

A. I know there was some mislabeling on these slides. I can't remember exactly what it was. All I know is that, when I reviewed it, I knew which one was which; specifically, what the right lower lobe biopsy was from the left upper lobectomy specimen.

Q. Now, the slides that you did review were recuts; is that right?

A. Yes.

Q. What is a recut, briefly?

A. When tissue is processed pathologically, it's put into a plastic cassette and put through an automatic tissue processor and that tissue is eventually embedded in paraffin. That makes what is called a paraffin block, and that paraffin block contains the tissue from which the very dense slices are made which are put on glass slides and then

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stained.

Initially, you have an original set of slides that the pathologist looks at. There are certain instances in which you want to have additional sections cut from that block, and those would be referred to as recuts.

There are a number of different reasons you want to have recuts made. Sometimes it's so another pathology can see exactly the same material and the treating institution retains the slides. Other times it's because you want to go deeper in the block to see if you find anything different than was seen in the initial sections. Sometimes the recuts are made to have special studies on them like histochemistry and immunohistochemistry.

Q. It's fair to say that the slides you received were recuts?

A. I believe they were, yes.

Q. They were not the original slides that Mr. Little's pathologists who treated him or were involved in his treatment looked at when they reviewed his pathology?

A. I think they were recuts to be quite honest, although I really can't say for certain. I think they were.

Q. If they were, I take it you did not ask if the originals were available?

A. I didn't. Most of the time the recuts are going to be very similar to the original because the

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distance between where the original slide was made and the recut is very small.

Q. One thing I wanted to clear up before we got too much further down the line because we started talking about where the pathology came from.

I wonder if you can look at Exhibit 3 which was your cover letter to Mr. Patrick.

A. All right.

Q. I think in the second paragraph you talk about the chest radiograph showing an abnormality in the left lower lobe. Do you see that?

A. I do.

Q. If you look at Exhibit 4, which is your report, the second paragraph on the first page notes that a chest radiograph showed an abnormality in the left upper lobe?

A. That's my error. That should have been left upper lobe.

Q. Okay. In the letter to Mr. Patrick?

A. That is my error. I didn't catch that.

Q. You got that information from Dr. Harley's report, I take it?

A. That and from the pathology report.

Q. From the pathology report?

A. Right.

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Q. You haven't seen the radiology report that described an abnormality in the left lower lobe?

A. No. I think the abnormality, according to Dr. Harley's report and the pathology report --

Q. Excuse me --

A. -- was in the left upper lobe.

Q. -- left lower lobe. I read the wrong thing.

A. It was my error. For reasons I can't remember, I put left lower lobe.

Q. You didn't see the radiology report that described it?

A. I did not.

Q. And you didn't see the original radiology either?

A. No.

Q. Now, you reviewed the pathology slides that were sent to you, correct?

A. Yes.

Q. Did you take any photomicrographs?

A. I did.

Q. And do you have those with you?

A. I do.

Q. I take it you only have one set of those?

A. I do.

Q. You went and you got, what is it, three total

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sheet of photomicrographs there?

A. There's a total of 48 two-by-two projection slides.

Q. Can you describe for me what those 48 slides are of?

A. Sure. They are of the tumor that was present in the resected left upper lobe. The surgical pathology number designated to that was S996-4435, and they are photographs of the biopsy that was done from the right lower lobe. The surgical pathology number on that was 96-16688.

Q. You took all of those photomicrographs from your review of the slides that were sent to you?

A. No, not all of them. I took them from review of some of the slides that were sent to me and also the slides that we made in our laboratory that represented the immunohistochemical stain sections.

Q. So some of those were taken after the staining was done?

A. Yes.

MR. MURPHY: Jerry, we can talk about this off the record further; but if there's a way we can get copies of the photomicrographs, we would certainly like to have those.

MR. EVANS: Okay. We'll discuss it at the next break.

MR. RILEY: We would also like a set.

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THE WITNESS: It's simple. We'll just make duplicate copies. Two sets of duplicate sizes.

MR. MURPHY: We can work through Jerry to get them.

THE WITNESS: I'll send them to you.

MR. EVANS: Okay.

(Request for production.)

Q. BY MR. MURPHY: Doctor, in terms of making the slides, it would be a fairly simple process?

A. Very simple.

Q. You would have no objection to having slides made for us?

A. Not at all.

Q. Is that a process that takes a long time, Doctor?

A. I guess it depends on how you define long, but I would say not very long. Sometimes it's as short as a day and up to three days as a maximum. A pretty short time.

Q. In terms of your schedule is there any reason why there would be a significant delay before we could get a copy?

A. No. I can actually take these to the photography place that I have this done at tonight, and I could probably have them back at the latest on Wednesday and maybe even Tuesday.

Q. That certainly would be great if you could do

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it.

In terms of the slides, you did receive the slides that were already prepared. When you received them, you looked at them under a microscope; is that right?

A. Yes.

Q. You did that for the purpose of determining yourself, I guess, No. 1, whether they represented cancerous cells; and, then, No. 2, what the cell type was. Is that fair to say?

A. That was one thing I looked at. The thing I think all pathologists would do in this situation is try to read the pathology report corresponding to the slides to understand what specimens are removed and then kind of match up the slides that you have with the pathology report and go through those in a systematic way.

Q. Would you agree with me that diagnosis of the cell type of a tumor is generally not made by gross observation of the tumor?

A. I'd agree with that, yes.

Q. Is it true you can't reliably diagnose a tumor as being any certain cell type based on the size of the tumor?

A. That is also true.

Q. When you looked at these under a microscope you used light microscopy?

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A. Yes.

Q. Do you have an electron microscope in your lab?

A. Yes.

Q. But you didn't use it in regards to Little?

A. No.

Q. Now, when you looked at these recut slides under your microscope, you made a determination of the cell type of cancer they represent or the ones that did represent cancer; is that fair?

A. I did.

Q. Your determination was -- why don't you go ahead and describe what your determination was?

A. In the tumor that was present in the slides designated as SP-4435, I thought the tumor had the features of either a poorly-differentiated squamous cell carcinoma or a poorly-differentiated adenosquamous carcinoma.

Q. That's the left upper lobe?

A. That is the left upper lobe, yes.

Q. Now for the right lower lobe?

A. In the right lower lobe, the tumor was partly differentiated, and I couldn't give an exact cell type other than to say that it was a non-small cell carcinoma.

Q. Is it fair to say, for all the slides that you looked at and all the tumor cells that you observed, that

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there is no doubt you observed a non-small cell cancer?

A. I agree with that. There's no doubt that this is a non-small cell cancer, yes.

Q. Is it fair to say that as far as you know that every pathologist who has looked at this pathology has agreed with that determination?

A. Yes.

Q. That includes Drs. Harley and Roggli?

A. Yes.

Q. And it includes the doctors at the hospital who were involved in the treatment of Mr. Little?

A. Yes.

Q. It would also include the defendants' expert that I guess Mr. Patrick told you about?

A. Yes.

Q. But pathologists have disagreed in terms of breaking the cell type drown from there; is that right?

A. I would say the only disagreement of any significance would be the diagnosis that was made -- at least that I was told was made by your expert. Other than that, I don't think there is any significant disagreement.

Q. Well, Dr. Harley -- I know I marked his report there in front of you --

A. Uhm-hmm.

Q. -- thought that the cell was large cell,

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didn't he?

A. Yes.

Q. And so did Dr. Roggli; is that right?

A. Let's make sure. (Perusing.) Yes.

MR. MURPHY: To further complicate matters, let's mark this 11.

(Defendants' Exhibit 11 was marked for identification.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you a copy of what has been marked as Exhibit 11 to your deposition. Would you identify that for the record?

A. That's a report by Dr. Allen Gown.

Q. This is a report on the slides that you had sent to him for surfactant ApoA1 immunostaining?

A. Yes.

Q. Dr. Gown examined the slides that you sent over to him and made a finding regarding cell type, didn't he?

A. Yes.

Q. His finding was that they were poorly-differentiated carcinoma; is that right?

A. Yes.

Q. That's an even different diagnosis than Dr. Harley or Roggli?

A. It's different words, but I think that, when you look at the context of the classification, the

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significance of difference between a poorly-differentiated carcinoma, a large-call differentiated carcinoma, a poorly-differentiated squamous cell carcinoma, and a poorly-differentiated adenosquamous carcinoma is very little.

Q. In any event, Dr. Gown didn't call this a large cell carcinoma?

A. No. Again, large is somewhat in the eyes of the beholder. If you want to get into the specifics about what is large, probably the best term, if you look at the classification of lung cancer, is that 40 percent of the cells have to be over 40 micrometers in diameter to call it a large-cell undifferentiated carcinoma.

I don't think pathologists often get that specific, and the reason they don't get that specific is that the treatment given for lung cancers is basically based on the designation of either small cell or non-small cell. There may be some variation between, say, adenocarcinoma versus squamous carcinoma, especially because adenocarcinoma usually is treated with chemotherapy whereas squamous carcinoma -- again, depending somewhat on its mutation -- is often treated only with radiation therapy.

Q. But the WHO pamphlet that you brought with you today does make a distinction between large cell and squamous cell and adenosquamous; is that right?

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A. It does. The primary difference between, say, large-cell undifferentiated carcinoma versus adenocarcinoma or squamous is that the large-cell undifferentiated carcinoma shows no histologic evidence of squamous differentiation.

Q. From what Dr. Roggli and Dr. Harley saw, they felt comfortable calling this a large cell?

A. They did, yes.

Q. And Dr. Gown didn't?

A. Dr. Gown called it a poorly-differentiated carcinoma. That's kind of a wastebasket term. Most of the time, when a pathologist says that, they would mean a non-small cell lung cancer. I guess you would have to ask Dr. Gown what he meant by that.

Q. You haven't asked him?

A. No. But I've been around pathology long enough, especially with lung cancer, that most of the time, when somebody says poorly-differentiated carcinoma, they really mean undifferentiated carcinoma or they mean that they can't be absolutely certain whether the tumor is showing any squamous or glandular differentiation, but they are certain that it's not a small cell carcinoma.

Q. You haven't asked or talked to Dr. Roggli or Dr. Harley about what they meant when they called it a large cell?

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A. No. But that's, again, petty well defined as a tumor that is composed of what pathologists perceive as large cell that shows no squamous or glandular differentiation. I thought that this tumor definitely showed squamous differentiation, as did one of the treating pathologists if you look at their report and additional biopsy specimen.

Q. That's the specimen that you didn't review?

A. That's true.

Q. So you are not sure exactly what it was that they saw that made them come to their conclusion that it might represent a squamous cell?

A. I didn't, but there are very strict criteria for squamous carcinoma. That's what I thought I saw in this case, and those criteria are two things: One is that there is definite evidence of keratinization; and, two, there's definite evidence of intercellular junctions between the tumor cells.

I thought you could see both in this case, and I took photographs to show that. I would also say, from a practical point of view, it doesn't make any difference.

Q. You mentioned a couple of things that I want to try and catch up on. The treating pathologist, who listed a diagnosis of squamous cell -- and I think we are talking about what we've had marked at Exhibit 8 -- that was

http://legacy.library.ucsf.edu/tid/tpb50f00/pdf Source: https://www.industrydocuments.ucsf.edu/docs/tgxl0001

from pathology taken from the anterior mediastinal node; is that right?

A. That was the initial biopsy specimen that rendered this man initially a nonsurgical candidate.

Q. There was a biopsy taken from the left upper lobe lesion?

A. There was.

Q. That biopsy was not diagnosed as squamous cell?

A. No, but that's exactly my point. That was diagnosed as a poorly-differentiated carcinoma, non-small cell type. If you were to look at all squamous carcinomas of the lung that were poorly differentiated, you could find areas in that tumor where you could not differentiate that tumor as a squamous cell carcinoma.

That goes back to the classification of lung cancers, and that is that you classify it by the best differentiated area and you grade it the worst. If you see a lung cancer that has any areas of squamous differentiation, then that's squamous cell carcinoma. If you say that the majority of the tumor is poorly differentiated, then it's a poorly-differentiated squamous cell carcinoma.

Q. I guess what I'm getting at, though, in Exhibit 8, in the two different diagnoses, they didn't come from the same tumor, did they?

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A. No. But I think that also goes to show you what lung cancers often do, as do many other tumors. They show variability in differentiation, and you can have areas in a squamous carcinoma that's even well differentiated where it might also be poorly differentiated.

Q. Do tumors also de-differentiate?

A. I'm not sure exactly how you -- it depends on how you define de-differentiate. I don't know how you define that. What do you mean? I can't answer that question unless you can tell me what you mean by de-differentiate.

Q. Well, do tumors exhibit mutational instability as they progress?

A. Yes.

Q. Is it possible, on an initial diagnosis of a tumor, to appear as one cell type and then later, when additional pathology is taken, for it to appear as another cell type?

A. That's possible but not common, and it would also depend to a certain degree on if there had been any treatment of the tumor and what the initial cell type was and how many sections were taken of the initial tumor.

Q. Just to make clear what we talked about a minute ago, the squamous diagnosis from the treating pathology came from the lymph node biopsy and not lung

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tissue; is that correct?

A. Right. But you have to realize -- and I'm sure you do -- that that tumor in the lymph node didn't grow there initially as a primary tumor. That represented a metastatic tumor from the primary lung cancer. If that tumor showed evidence of squamous differentiation, the tumor in the lung also showed squamous differentiation. Whether or not somebody saw that or not is a whole other issue.

Q. One of the things you mentioned about for histological diagnosis of a squamous cell carcinoma was intercellular junctions between tumor cells?

A. Yes.

Q. Is that what they call prickles?

A. Yes. Prickles are the best developed form of that.

Q. Correct me if I'm wrong, but I didn't see a description of intercellular junctions between tumor cells in your report as a description of what you saw.

A. You probably didn't. Maybe I didn't even say it, but I still think this is a squamous carcinoma based on what I saw.

Q. Do you recall seeing intercellular junctions between tumor cells?

A. I do. I did.

Q. But you just didn't note it?

http://legacy.library.ucsf.edu/tid/fra00/pdf Courtesy of www.industrydocuments.ucsf.edu/docs/tgxl0001

A. I probably noted in my mind. I probably didn't write it down.

Q. By the way, did you take any notes or record anywhere else what you were observing as you looked at the slides through the microscope?

A. No.

Q. Anything you have written about the Little case is in your file which you have?

A. Yes.

Q. Are there any of those photomicrographs that -- I notice you are holding them up -- you can identify for us today that would show intercellular junctions between tumor cells?

A. I think so. I'd have to project them. I can't see well enough here. The other thing that really shows that this is a squamous cell carcinoma is the one of the immunostains that I did.

Q. We are going to get to that. I guess I want to look at that observation under the microscope first.

A. I think there would be. I think that you can see intercellular junctions if you projected these slides, but I can't say just looking at them and holding them up.

Q. You have recollection of slides showing focal areas of keratinization?

A. Yes.

http://legacy.library.ucsf.edu/tid/tgx00/pdf www.industrydocuments.ucsf.edu/docs/tgxl0001

Q. Can you say from holding them up, or do you have any recollection of which slides they were?

A. I think there is a slide that's designated No. 21, March 4, 2000. I think that's the best one of them.

MR. RILEY: May I see those for a second?

THE WITNESS: Sure.

MR. EVANS: (Perusing.)

Q. BY MR. MURPHY: Doctor, I know you have talked in the past about interobserver variability among pathologists, correct?

A. Correct, yes.

Q. The point simply -- I guess I don't want to put words in your mouth -- is that different pathologists can disagree to some extent about what they view under the microscope?

A. Yes.

Q. In fact, good pathologists can have honest intellectual disagreements about what they can see; is that fair?

A. Yes.

Q. You wouldn't necessarily question a pathologist's motives if he came to a different diagnosis of cell type than you?

A. No.

Q. There is even such a thing called

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intraobserver variability, isn't there?

A. There is.

Q. That's when the same pathologist views the same pathology at different times and formulates a different diagnosis; is that right?

A. Yes.

Q. Has that ever happened to you?

A. I'm sure it has. I think It's happened to every pathologist. I think the more experience you get probably the more you looked at a certain type of thing you're interested in, the less intraobserver variability there is. I think as time has gone on in the criteria for diagnosing certain types of lung tumors it becomes more concrete and there's less intraobserver and interobserver variability.

Q. But in any event, in treating patients, pathologists can and do disagree about things like the cell type of cancer?

A. They do disagree, and that's, I guess, where the role of immunohistochemistry becomes important or potentially important. I think you have to look at it with respect to whether the disagreement is going to make a difference in how the patient is going to be treated. Sometimes it will, and sometimes it won't.

In the case of lung cancer, the most important thing,

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as I've said already, is that it's between small cell and non-small cell. That's usually all the clinical doctors want to know -- and specifically an oncologist -- but sometimes that's not totally true because they would treat like an adenocarcinoma different from a squamous carcinoma.

Q. Let's talk a little bit about the slide cutting that was done on the blocks you received.

A. Okay.

Q. That was done at your lab; is that correct?

A. We cut some of the blocks. Specifically, I think it was SP96-4435. I think it was F4 and F5, and it was 96-16688. We cut one of those blocks as well.

Q. Those are the three blocks you cut from?

A. Yes.

Q. I guess for staining at your lab you cut seven slides from each of those blocks; is that right?

A. (Perusing.) Yes, I believe that is correct. We performed an H&E stain, a Movat stain, and then immunostains for low molecular weight keratin, high molecular weight keratin, keratin 5/6, keratin 7, and thyroid transcription factor I. I think those were what we cut from each of those blocks.

Q. And then two additional slides were cut from each block where the staining was done by PhenoPath Lab and Dr. Gown?

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A. Correct.

Q. So a total of nine stains were cut from each block?

A. Yes, that's correct.

Q. Twenty-seven total slides were cut?

A. Right.

Q. How did you make the determination that it was appropriate for you to cut slides from these blocks?

A. Well, I guess I made the determination based on my experience as a pathologist and based on what I thought the histologic appearance of the tumor was in the H&E stain sections, and I wanted to see if that could be proven by the immunostains. Those are the ones that we performed at our laboratory.

The immunostains that were asked to be done for surfactant apoprotein A-1, I cut those at the request of Mr. Patrick and Dr. Harley.

Q. In terms of the appropriateness of cutting the blocks, did you rely on the plaintiff's counsel's request?

A. No. I guess I relied on my own experience as a pathologist and what I thought the tumor looked like.

Q. I guess I'm getting at maybe a different question.

A. Okay. I don't understand, then. I'm sorry.

Q. When you cut slides from the blocks, you

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change the nature of those blocks; is that right?

A. Can you say that again, please?

Q. It's a fairly general question. Maybe I need to take it through some specifics.

When you cut the blocks you change the nature of the blocks?

A. I guess you can say that that is correct. You take a very thin slice of tissue off of the block once you have faced the blocks so you can get a purely perpendicular cut. The amount that I change those blocks would be minimal, but I would change those. Everything I prepared from those blocks and did change the blocks is available for somebody else to look at. The only thing that they could not look at would be the tissue that was removed that was necessary to face the blocks to get a purely perpendicular cut.

Q. It's fair to say that there is now less tissue left on the blocks?

A. There is less tissue but not a great deal less tissue. The sections that we cut in our laboratory for H&E stain sections and immunohistochemical stain sections are three micrometers thick. We cut very thin slides because I like it that way so you can see the morphology best. The amount of tissue that we remove from those blocks by doing these additional stains is minimal.

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Q. Now, the slides that you cut and stained, while they can be viewed by others now, they can't be restained?

A. Actually, they could be restained if you really wanted to do it. It wouldn't be indicated, but they could be restained. I've done it many times. There wouldn't be any reason to do so.

Q. You say it wouldn't be indicated. What do you mean by that?

A. Because there is still tissue left in the blocks and you could cut some more recuts. Again, the basic idea is that when you make this thin section there is going to be very little change from one slice to another.

Q. Can you state with any certainty that the tissue that remains on the blocks contains tumor cells similar to the original pathology slide?

A. I think you can say it with a fairly significant degree of certainty that it would, yes. I think the chances of it would be highly likely. I don't think there's going to be any big change in cell type. There's always a chance that you might find something a little bit different, but in general it's going to be the same.

Q. It's fair, though, to say that cutting slides is destructive testing?

A. I wouldn't consider it destructive testing, I

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guess, unless you define what you mean by destructive. To me, it's something you do to basically make a diagnosis or gain more information concerning a case. Sure, you destroy part of the tissue there, but you preserve part of the tissue and you do things on the sections that you made that are going to provide insight into understanding the case.

Q. You understand now and you understood when you cut the slides that this case was in litigation?

A. I did, sure.

Q. You understood that there's another side to the case, besides the plaintiff's that there's the defendants'?

A. Of course. I always understand that.

Q. It would only be fair, should they choose to do so, that the defendants' have the opportunity to do staining or any cutting that they feel appropriate?

A. Absolutely.

Q. Did you consider, when you cut the 27 slides, nine from each block, that you should cut extras to preserve some of those for any testing that the defendants might want to do?

A. I'm pretty sensitive about that because of the asbestos litigation I have been involved in for many years. If I thought there was any way there would not have been any tissue left in the block for your side to look at, I would

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have made sure that there were some extra slides of unstained tissue kept. There was plenty of tissue left in those blocks and there are additional blocks that have tumor that the defense or anybody else could do additional sections on.

I would never --

Q. I'm not trying to say that you did it. I'm just asking whether you considered, instead of cutting all the slides and leaving us further down the block, alternating and cutting some that you didn't use preserved during the course of you cutting your slides.

A. I always consider that when I think there's an insufficient amount of tissue and only a minimal amount of tissue present. In this case, if you look at how many we cut -- 9 times 3 is 27 -- that's 27 micrometers. A micrometer is one one-hundred thousandths of a meter, one one-thousandths of a millimeter. It's a very, very thin piece of tissue, and in that number of pieces of tissue that made those nine slide there's not going to be any significant loss of tissue.

Again, if I thought there would have been any way that we destroyed the block that your side could not look at it, I would have done everything in my power to make additional slides for you or anybody else to use.

Q. Now, Doctor, if you were diagnosing cancer in

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a patient in your hospital and pathology existed that was taken before the patient received chemotherapy and radiation treatment and pathology existed after chemotherapy and radiation treatment, would you want to see both of those?

A. You would, yes.

Q. Chemotherapy and radiation treatment can alter the appearance of cancer cells, can't they?

A. They can.

Q. It can also alter the appearance of normal cells?

A. Yes.

Q. Pathology texts warn against mistaken diagnosis based on pathology taken after chemotherapy and radiation treatment, don't they?

A. They do.

Q. Are well-differentiated BAC cells resistant to radiation therapy?

A. I don't think of the BAC as being a very radiation-sensitive tumor, but that's not to say that the cells of the bronchioloalveolar cell carcinoma are not going to be changed by radiation, because I think they are and I think that's observed in people who receive radiation where you get lung biopsies and you can see changes in those cells.

I don't think that those are cells that are typically

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radiation sensitive. They frequently undergo hypertrophy and hyperplasia and become atypical in people that have been irradiated.

MR. MURPHY: Let's off the record.

(Recess taken.)

Q. BY MR. MURPHY: Doctor, pathologists who reviewed Mr. Little's lung tissue as part of their treatment at the hospital made their diagnosis without staining any of the lung tissue; is that right?

A. Yes.

Q. Were they wrong to do that?

A. No. I would have done exactly the same thing. I would not have done any special testing on this case had it been a case that I would have seen at the hospital.

Q. Now, Drs. Roggli and Harley looked at this case for litigation purposes, and they made a diagnosis of a cell type of cancer without any staining, correct?

A. Right.

Q. Were they wrong to do that?

A. No.

Q. Defendants' pathologists have looked at this lung tissue and made a diagnosis without staining, to your knowledge; is that right?

A. I don't know about that.

Q. If they did, were they wrong to do that?

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A. Nobody would be wrong to do no staining on this case.

Q. Was staining necessary in this case?

A. From a treatment point of view, no.

Q. Was it necessary from the point of view for you to be able to make a diagnosis of cell type to a reasonable degree of medical certainty?

A. No.

Q. It was not necessary to do?

A. It was not necessary.

Q. Tell me, why was staining done in this case?

A. I did it in this case because I was told that your pathologist or somebody who reviewed the material for you was saying that this tumor was a bronchioloalveolar cell carcinoma, and to me the tumor histologically did not have that appearance and I wanted to do the immunostains to provide additional support that this tumor was not a bronchioloalveolar cell carcinoma. That's also why Dr. Harley asked for the immunostains to be done for surfactant apoprotein.

Q. Is it fair to say that the staining was done in this case not for purposes of coming to a diagnosis but for purposes of excluding the defendants' diagnosis?

A. Yes, that is correct.

Q. Would you agree with me that

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immunohistochemistry is not necessary for the diagnosis of BAC?

A. I would agree with that, yes.

Q. Would you agree with me that the immunohistochemical features of BACs are similar to those of other adenocarcinomas of the lung?

A. In general, yes.

Q. Do you agree that BACs with Type 2 cell differentiation often stain with anti-surfactant antibodies?

A. Yes.

Q. Do you agree that BACs with Clara cell differentiation stain for Clara cell antigens?

A. Yes.

Q. We are going to talk about some of the staining that you did, but you didn't stain Mr. Little's lung tissue with Clara cell antigens, did you?

A. As far as Clara cell antigens, I'm not sure I understand exactly how you define what a Clara cell antigen is. I guess maybe you could get back to the point of exactly how you define what a Clara cell is.

MR. MURPHY: We may as well mark this because we might refer to it from time to time today. Can we have this as the next in order?

(Defendants' Exhibit 12 was marked for identification.)

Q. BY MR. MURPHY: I'm going to hand you what we

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have marked as Exhibit 12 to your deposition. Would you take a look at that and tell me if you are familiar with that?

A. I am familiar with that, sure.

Q. What is Exhibit 12?

A. It's what is referred to as an Armed Forces Institute of Pathology fascicle. This is the third series, and it's Fascicle 13, which is "Tumors of the Lower Respiratory Tract," that was written by Thomas V. Colby, C-o-l-b-y; Michael N. Koss, K-o-s-s; and William D. Travis, T-r-a-v-i-s.

Q. Let me stop you there for a minute. Drs. Colby and Travis, they are two of the doctors who you noted were included on the cover of the new WHO classification; is that correct?

A. Yes.

Q. My question about identification was a little bit unfair because you may not have known exactly what portion of the "Tumors of the Lower Respiratory Tract" fascicle this was, but it was Fascicle 13 for bronchioloalveolar carcinoma; is that right?

A. It is, yes.

Q. I just wanted to refer to you, at least for now briefly, to page 226.

A. Okay. (Perusing.) All right.

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Q. It's the second paragraph after the heading "Immunohistochemical Findings." Do you see that?

A. Yes.

Q. I'm really referring to the last portion of the second sentence of that paragraph. Just to try to summarize it: BACs with Clara cell differentiations stain for Clara cell antigens."

Do you see that?

A. Yes, I do see it.

Q. You agree with that; is that right?

A. I agree with that, but I think you have to define exactly what the Clara cell antigens are because I think you must realize -- or maybe you don't realize -- that many cells have all kinds of different antigens. I guess the Clara cell antigen would be -- are you talking about a secretory product of the cell? Are you talking about a substance that's on the subsurface that's not a secretory product? You have to define what you are talking about.

As far as I know there are not any commercially available antibodies against Clara cell antigens.

Q. Let's change gears and talk about the staining that was done to the pathology you received from Mr. Little's lung tumor, and it's what hopefully will be an aid to our discussions.

MR. MURPHY: I want to have this marked as next in

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order.

(Defendants' Exhibit 13 was marked for identification.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you what we have marked as Exhibit 13. It's titled "Summary of Dr. Hammar's Immunohistochemical Staining." I'll ask you to take a look at that.

A. All right. (Perusing.)

Q. What we have tried to do here was summarize in a chart the staining that was done out of your lab or Dr. Gown's lab, I believe, and the results received. Maybe we can walk through some of those.

A. Okay. (Perusing.)

Q. Now, the first stain we have listed on the chart is cytokeratin 5/6 stain. Do you see that?

A. I do.

Q. Why did you do the cytokeratin 5/6 stain?

A. Because cytokeratin 5/6 are the types of keratins that are present in the most squamous cell carcinomas.

Q. Let me try and back up for a minute. You stained slides from each of the blocks you received for cytokeratin 5/6; is that right?

A. No, not each of the blocks we received. We stained them on sections from block SP96-44345 F4 and F5, and 1668 I think was Block 2.

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Q. But you only received one block from -- those are the three blocks you received, right?

A. Those are the three blocks that we did the stains on, yes.

Q. Those are the only three that you received; is that right?

A. We received 16 blocks --

Q. I'm sorry.

A. -- designated SP96-4435. What I did was selected out the blocks that I thought had viable tumor that actually contained the most tumor evaluate.

Q. As the chart breaks down, it lists two different slides that you stained from F4 and F5?

A. Those are two different blocks, F4 and F5. We made sections from those which we did the immunohistochemistry staining on.

Q. Why did you stain two slides from F4 and F5?

A. Why did I use two blocks? Because there was some difference in the appearance of the tumor from one to another, and I just wanted to see the spectrum.

Q. Then you also did two slides from Block F4; am I right?

A. I don't --

Q. From F5?

A. I don't understand the point you are asking;

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I'm sorry.

Q. In your report you describe neoplastic cells --

A. Right.

Q. -- and then you describe reactive alveolar lining cells?

A. Right. But they are the same section. They are not two different slides. Those are all in the same section, and actually the reactive cells usually serve as the ability to control for at least some stains. That's one way you can determine if the immunohistochemical test is working properly.

Q. The reactive cells, you would agree, were enlarged?

A. Yes. You basically get reactive alveolar lining cells around virtually every lung tumor there is. That occurs in the periphery of the lung anyway.

Q. And this tumor occurred in the periphery, right?

A. It did, yes. It didn't, obviously, occur within a block, so it would be in the gas exchange portion of the lung parenchyma.

Q. If a tumor occurred within a bronchus, you would term it central; is that correct?

A. Not necessarily. You can have tumors that

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occur from small bronchi that are peripheral tumors. The tumors that occur within central bronchi are usually squamous carcinomas and small cell carcinomas.

Q. If you had to give your opinion on where this tumor occurred, would you describe it as a peripheral tumor?

A. I can look at all the reports to see exactly where they said it occurred. That's easy to do. Let me look and see what they say. (Perusing.)

Q. Without getting there necessarily, have you made your own determination of whether this was a peripheral tumor?

A. This was a tumor that was in the gas exchange portion of the lung parenchyma. I can't remember how close it was to the pleural surface, how far it was away from the bronchial margin of the section; I would have to look that up.

Q. Would that be something you would be able to observe on radiology?

A. Usually, yes.

Q. You haven't looked at any radiology to make that determination?

A. I have not.

Q. Would you rely on a radiologist for that type of information?

A. You could rely on a radiologist. The only

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thing you'd have to be careful about in a case like this is that according to the information that I had was that this tumor, I think, measured between an inch to two and a half inches in greatest dimension. Two and a half inches in greatest dimensions -- there's 2.5 centimeters in an inch.

If you multiply 2.5 by 2.54 -- what's that come to? It's 6.3 centimeters. A 6.3 centimeter tumor in the left upper lobe can almost extend from one pleural surface to another, so that it potentially could be a centrally located tumor or a tumor that arose from the bronchus. What you'd have to do is try to read the pathology report from whoever did the dissection to look very carefully if they saw any tumor within a bronchus because that's a good-sized tumor. That's a big tumor.

Q. What you are trying to do is determine from where the tumor arose not where it exists when you find it; is that right?

A. Well, practically speaking, it doesn't really matter where it arose from. What's most important is what type of differentiation it's showing, how you classify it so you can get it into the right treatment category. As we talked earlier, the most important designation is small cell versus non-small cell.

Q. Do peripheral tumors continue to grow centrally?

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A. Peripheral tumors in most instances stay in the peripheral lung. Again, I'm not sure there's a definite definition of peripheral other than it's using the pleural surface. But you can have central tumors that extend to the periphery of the lung and involve the peripheral portion of the lung.

To make the distinction of where the tumor began versus what part of the lung parenchyma it involves, you usually have to do a very careful dissection of the bronchial tree to see if there is any evidence that it originated in the bronchus, which can be difficult at times. Sometimes you can't say. All you can say is that this is the size of the tumor, this is what part of the lung parenchyma is involved, and this is what it looks histologically.

Q. Is it fair to say in this case that any information you have regarding whether the tumor was peripheral or not comes from the pathology report?

A. Yes.

Q. And you're looking at that now. Did you find the information that you are relying on in describing the location of the tumor?

A. Well, yes and no. For example, what it says is that the nodule approaches to within 0.6 centimeters of the pleura at the apex. And then it says a couple of sentences down, the tumor approaches to within 5 millimeters

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of the staple line. The tumor approaches to within less than 1 millimeter of the hilum. The hilum is basically where the blood vessels and large air tubes are.

Basically, this is what I'm trying to say: You have a fairly good-sized tumor in a relatively small portion of the lung. I don't know what the left upper lobe looks like, but you can have a tumor that does involve periphery but also can involve the central portion of the lung.

Q. Would it help in determining whether the tumor was peripheral or not to view older radiology which might show early evidence of the tumor?

A. That could help, yes.

Q. Do you know if any of that is available in this case?

A. I don't know.

Q. Now, we were talking about reactive alveolar lining cells and we got sidetracked onto a discussion of peripheral tumors.

Would you agree that reactive alveolar lining cells have hyperchromatic nuclei?

A. Yes.

Q. Would you agree that reactive alveolar lining cells have an increased nucleus to cytoplasm ratio?

A. Yes.

Q. Would you agree that the nuclei in the

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reactive alveolar lining cells show a coarse chromatin pattern?

A. They can, yes.

Q. Now, let's try to turn back to the staining in the chart. We started to talk about cytokeratin 5/6 staining.

Can you see where we have listed the results of that staining in the chart?

A. I can.

Q. Do you agree that -- I guess you agree that the chart accurately depicts the results you received?

A. It believe it does, yes.

Q. There was a slight positive reaction in the neoplastic cells in F5?

A. Yes.

Q. And for all the other cells it was negative?

A. Yes.

Q. So if cytokeratin 5/6 is a good squamous cell marker and there was only a slight positive reaction in one of the cells that you stained, would this be evidence pointing away from this cancer being a squamous cancer?

A. No. We actually stained more than one cell. We stained several cells. I can show you these photographs if you'd like to look at them of cytokeratin 5 and 6. Those are on the tumor in F5.

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Q. I don't want to look at them here.

MR. EVANS: Can we I get the number on the record?

THE WITNESS: This is numbered as Martin -- it's labeled as Martin Little, SP96-4435, and it's slides No. 17 and 18.

MR. EVANS: And No. 17 and 18 are your numbers?

THE WITNESS: No, the numbers on the slides.

MR. EVANS: Okay. But the slides you brought today are all numbered?

THE WITNESS: Yes, they're 0072.

MR. EVANS: The numbers 17 and 18 are part of the sequence of numbers?

THE WITNESS: Those are part of the sequence of the photographs I took.

MR. EVANS: In other words, those are your individual numbers?

THE WITNESS: Right. When I take photographs I write it down on one of these little cards like this what I take it of, and that's how I keep track.

I mean, if somebody goes back and looks at these slides, they're available.

MR. EVANS: When you make our sets could you number our slides --

THE WITNESS: Oh, yes.

MR. EVANS: -- so our 17 will correspond with your

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17?

THE WITNESS: Sure. I will definitely do that.

Q. BY MR. MURPHY: Now, why did you do the cytokeratin 7 stain?

A. Cytokeratin 7 is a marker of a primary lung cancer, and it's seen most frequently in adenocarcinomas but it's also seen in some squamous carcinomas, can be seen in large cell differentiated carcinomas, and it could be seen in occasional neuroendocrine carcinomas like small cell carcinomas.

That was done primarily to prove that this was primary lung cancer, and the reason I did that was primarily because of the Butler case where the pathologist on your side stated that his cancer was a metastatic tumor from the pancreas. I just wanted to kind of get that out of the way, so to speak.

Q. You had no indication that anyone on the defense side claimed that this was not a primary tumor, did you?

A. I did not. But the same thing was said in the Butler case until about two weeks before trial when all of a sudden the tumor in his lung, that was said by your side to be a primary tumor, all of a sudden became a metastatic pancreatic tumor. But, no, I did not.

Q. The fact that cells stain positive for cytokeratin 7 does not help us in distinguishing the tumor

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being an adenocarcinoma or a squamous cell, does it?

A. Generally, it's relatively uncommon to see cytokeratin 7 as squamous carcinomas, but it does happen. I would say that about 20 percent of them stain positive for cytokeratin 7.

Q. So this would have to be one of those 20 percent?

A. Yes.

Q. Why did you do a low molecular weight keratin stain?

A. Because most adenocarcinomas, including bronchioloalveolar cell carcinomas would stain positive for low molecular weight keratin, and that specifically refers to an antibody that's referred to as 35BH 11 produced by Dako. That antibody was actually produced by Dr. Allen Gowen here in Seattle.

Q. As our results in this chart lists -- correct me if they don't reflect what your results were -- the F5 reactive cells and the B2 sample did stain positive for low molecular weight keratin; is that right?

A. That's correct, yes.

Q. Does that information help in concluding whether this tumor was an adenocarcinoma or a squamous cell?

A. It's not absolute. All I can say is that over 90 percent of adenocarcinomas that I've seen in the lung

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stain positive for low molecular keratin. If you look at the profile of keratins in adenocarcinoma of the lung and look at the keratin subtypes BH35 and BH11 antibody stains, most adenocarcinomas of the lung would be positive.

Q. So the results from the low molecular weight keratin staining support the diagnosis of adenocarcinoma?

A. No, they don't. They would not support it. They would prove against it. This is not absolute. This is not absolute, and the most important thing to remember about immunohistochemistry.

Q. None of these stains that you did or Dr. Gown's lab did are absolute?

A. They are not absolute, but the best ones on this chart you have not gotten to yet -- the most specific.

Q. Okay. We are going to work to them.

If I were trying to garner information in support of a diagnosis of adenocarcinoma, could I point to the positive results for the low molecular weight keratin stain?

A. You could point to that as a strong supporter of the diagnosis of adenocarcinoma, yes.

Q. Why did you do high molecular weight keratin stain?

A. Because that usually stains squamous cell carcinomas. That antibody is referred to as 34B 12. It can stain some adenocarcinomas as well. It's not specific, but

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it would stain squamous carcinomas more frequently than adenocarcinomas.

Q. But it does stain adenocarcinomas?

A. It does stain some, yes.

Q. You have a chart in your book that indicates that both squamous and adenocarcinomas express high molecular weight keratin, right?

A. That's correct.

Q. What type of high molecular weight keratin did you use?

A. Antibody 34B 12. I'm trying to think of what keratin that is. It would be one of the ones between 1 and 8. It would not be 8 because it is a low molecular weight keratin. It's a high molecular weight keratin, and I think there's a molecular weight of about 68,000 kilodaltons.

Q. Do you know the manufacturer of the stain you used?

A. Yes, Dako.

Q. Why did you do the thyroid transcription factor I stain?

A. Because that is the most specific stain for adenocarcinomas of the lung there is. That is present, in my own experience, in up to 75 percent of adenocarcinomas. It's a nuclear stain. It's one that is easy to use and one that usually you have built-in positive control staining.

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Q. Do you have any opinion on what percentage of BACs would positively stain for thyroid transcription factor I?

A. The ones that I have seen, 100 percent. The reason for that is that the transcription factor that that codes for is actually for surfactant. It's a transcription factor, and transcription has to do with what copies the DNA and the nucleus.

Q. The reactive alveolar lining cells in Mr. Little's lung tissue were positive for thyroid transcription factor I staining, correct?

A. Yes.

Q. When we talked about these things as we are going through the chart, you and I have been talking about adenocarcinoma, correct?

A. Yes.

Q. Would you include BAC as a subset of adenocarcinoma when we talk about it?

A. Yes.

Q. You agree that BAC is a subset of adenocarcinoma?

A. Yes.

Q. And that's reflected in the WHO pamphlet you brought with you today?

A. Yes.

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Q. Now, would you agree that thyroid transcription factor I staining can be positive in large cell carcinomas?

A. Yes. But I think that is a reflection on what both large cell and differentiated carcinomas of the lung are, which usually is adenocarcinoma in most instances but not all.

Q. Could TTF-1 be positive squamous cell carcinoma?

A. Not according to what's been published so far. I've never seen it myself, and I've done a lot of tests to try to see that. As far as I know from the spec sheets that are published by the company that makes this antibody -- we use Biocare Medical -- no squamous carcinomas have been reported positive.

Q. Am I right that TTF-1 is almost always positive in small cell lung cancer?

A. It is. I would say that in every one I have looked for it also is a transcription factor for a neuroendocrine product.

Q. Is it fair to say that TTF-1 is not a very specific marker?

A. No, it's not fair to say that. It's one of the best and most specific markers we have at this point in time. It's the best single marker for diagnosing

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adenocarcinoma of the lung, and it may be best close to the best specific marker for diagnosing small cell carcinoma of the lung assuming that that tumor has a histologic appearance consistent with small cell.

Q. Is the fact that the F4 reactive cells and F5 reactive cells stain positive support a diagnosis of adenocarcinoma in this case?

A. No. Those are active cells; they're not malignant.

Q. Can you tell me why the reactive cells might stain positive but what you call the neoplastic cells stain negative?

A. Yes, I can tell you why.

Q. Why would that happen?

A. Because the neoplastic cells are not an adenocarcinoma and the reactive cells are cells for a surfactant. That's what that transcription factor is really coding for is surfactant.

Q. Why did you have Allen Gown's lab do the surfactant apoprotein A-1 stain?

A. I did not have them do that. I was just following instructions by Mr. Patrick to have that done.

Q. If you had to make a determination as to whether that was necessary in this case, would you have it done?

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A. The only reason I would have had it done would be because of what I was told that the defense said this tumor was. I think that's the reason it was done and that was because we were told your side said it was bronchioloalveolar cell carcinoma. Since that tumor frequently produces surfactant and that's what normal Type 2 pneumocytes do, that is a reasonable type of testing to do.

Q. So you would agree that surfactant apoprotein A-1 can be positive in adenocarcinomas?

A. Yes.

Q. Would you agree that thyroid transcription factor I is a more sensitive marker for adenocarcinoma than the lung surfactant proteins?

A. I don't think it's any more sensitive. I think it's maybe more specific. The only thing I know of that surfactant apoprotein stain -- and that's not A-1. There's actually, I think, three surfactant proteins and maybe even four now. I think there is A, B, C and D. There have been some reports that surfactant apoprotein B stains for breast cancers; but as far as I know surfactant apoprotein A can stain only lung cancers, but it does not stain 100 percent of adenocarcinomas of the lung.

Q. Is there a difference in surfactant apoprotein A-1 staining pattern for BACs with Type 2 pneumocytes compared with BACs with Clara cells?

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A. I don't know. I'd have to look that up. Clara cells actually produce a surfactant type of molecule similar to Type 2 pneumocytes, and I don't know whether the actual aminoacid sequence or the glycoprotein configuration of the surfactant produced by Type 2 pneumocyte Clara cells is the same. I don't know. I'd have to look that up.

Q. Where would you look for that information?

A. There's been a great review article written recently on Clara cells, and I think it was in the American Review of Respiratory Disease. I think it was written by Dr. Singh -- spelled the same way as the guy who won the Master's yesterday.

He wrote a very nice review article that talked about the whole history of Clara cells. That's where I would start because I think he has about 20 or 30 references in that review, and I think it would tell that information.

Q. Now, you also did a chromogranin A stain?

A. I only did that on the B2 slide, and that was because there was some suggestion, I think, by somebody that this could have represented a small cell carcinoma.

Q. Do you know who made that suggestion?

A. I don't know.

Q. The B2 slide was the slide of the tumor in the right lower lobe?

A. Yes, right lower lobe.

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Q. What does the results of that stain tell you?

A. It tells you that at least it's not producing a significant number of neuroendocrine granules because chromogranin A is a substance that is present -- it's a protein present in the neuroendocrine granules.

Q. Can you rule out that tumor in the right lower lobe being a small cell based on that stain?

A. Not specifically on that stain, but I think the two stains together, the chromogranin and the synaptophysin, you can say with a high degree of certainty it's not a small cell lung cancer and you can also say it's not a neuroendocrine carcinoma. It did not, to me, look like a small cell cancer at all. It's a non-small cell cancer.

Q. Why did you do the Movat's pentachrome stain?

A. I just wanted to see if I could get a feeling for where the cancer was located. In those two slides they were designated as -- or the sections from the block is designated SP96-4435 F4 and F5. That's a lasting tissue stain, and it gives you a beautiful picture on a slide or a stain that kind of shows where the elastic tissue is at, where the vessels are at, where the tumor is at. I just wanted to see what that was.

Q. What did that staining tell you?

A. It didn't tell me much in this case. There

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was so much fibrosis and reactive changes around the tumor, probably related to the therapy, that it wasn't very helpful.

Q. You felt the chemotherapy and radiation treatments altered the cells in such a way that that staining wasn't helpful?

A. I don't know if they altered the cells. They obviously killed a significant amount of the tumor because the tumor shrank, but the radiation and chemotherapy together frequently produce fibrosis -- scarring.

Q. Am I correct that you did not do the Movat's pentachrome stain in order to attempt to distinguish the cell type between squamous cell and adenocarcinoma?

A. That is correct.

Q. It does not help us do that; is that correct?

A. It does not help us do that.

Q. Now, you have in your text a chart that describes immunohistochemical features of common lung neoplasms?

A. I do.

Q. Does the text you brought also contain that photograph?

A. It does.

Q. I know it's on page 1161 of the big test that I have. It's Table 3217 in Dail and Hammar

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Pulmonary Pathology, second edition.

A. I'll get it. It's coming up.

Q. First of all, your chart doesn't list immunohistochemical features of BAC, does it?

A. No, it doesn't.

Q. It only breaks it down to adenocarcinoma?

A. Right.

Q. And of the stains you performed on Mr. Little's tissue that are listed in the chart -- first of all, only low molecular weight keratin, high molecular weight keratin and chromogranin are included on your chart; is that right? Of the stains that you did.

A. Yes. This book was kind of before -- this table was actually before all of the different antibodies were developed against specific cytokeratin molecules, the thyroid transcription factor was not available when this book was published, and the surfactant antibody is still not commercially available. This is somewhat primitive compared to what's available nowadays.

Q. In any event, to try to sum up this point, of the stains that you performed on Mr. Little's tissue that are listed in your chart, only low molecular weight keratin, high molecular weight keratin and chromogranin are included; is that right?

A. That's right, yes.

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Q. According to your chart there's no difference between the immunohistochemical features of squamous cell carcinoma and adenocarcinoma for low molecular weight keratin, high molecular weight keratin and chromogranin stains; is that correct?

A. That's correct, yes.

Q. Doctor, is it common in the field of pathology to do mucin staining on malignant tissue to determine if the tissue represents an adenocarcinoma?

A. It is, yes.

Q. Did you do any mucin staining in this case?

A. I did not.

Q. Do you have mucicarmine stain in your lab?

A. Oh, sure. It's m-u-c-i-c-a-r-m-i-n-e.

Q. Why do you do a mucicarmine stain?

A. Because I didn't think it was an adenocarcinoma. I didn't see anything, at least histologically, that made me think that. The other thing is most BACs, at least with the non-mucinous type, would be mucicarmine negative, and I didn't see anything again histologically that looked like what I thought was an adenocarcinoma. I could have done that, but I didn't.

Q. You did other staining in order to determine or, I guess, to try to accumulate proof that this was not an adenocarcinoma?

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A. Right. The thyroid transcription factor I and the surfactant apoprotein are much more specific than the mucicarmine stains, but mucicarmine stains and other mucin stains are still done and they are useful.

Q. For example, you could do a periodic acid Schiff diastase stain on malignant tissue and determine if it's adenocarcinoma?

A. Yes.

Q. And you didn't do any -- can I use just PAS with diastase staining -- in this case?

A. I did not.

Q. You have that stain in your lab, don't you?

A. Yes.

Q. Is there any reason why you didn't do that in this case?

A. I guess the same reason that I didn't do the mucicarmine. I didn't think this looked like a adenocarcinoma. But it can still be done.

Q. Now, in your report -- before we get there, Doctor, we talked about the surfactant stains and their not being available commercially; is that right?

A. Yes.

Q. Are they not available commercially yet because they are not widely used?

A. I wouldn't say that because if you look at the

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literature -- and I just recently completed a chapter for a book called Confidence in Diagnostic Immunhistochemistry and I cite a fair number of references in there where surfactant stains have been used.

Certain people around the United States have them. They're usually gifts that are from the individuals in Japan who made them. They are supposedly commercially available from Dako in Japan, and I've been trying to see if we can get them. They are fairly commonly reported on in the literature, but nobody really has them. I should say only a few people have them to use in the diagnostic sense. Dr. Gown, for example, uses surfactant in a diagnostic sense, but he is sent cases by other pathologists who want him to make a specific diagnosis.

Q. Do you know if Dr. Gown got his stain as what you termed a gift from Dako.

A. Not a gift from Dako. He got it as a gift from the person who developed the antibody. That's my understanding, and I think that's correct.

MR. MURPHY: Let's go off the record.

(Recess taken.)

Q. BY MR. MURPHY: Doctor, in your report you talk about -- one of the places you do this is your summary statements. It's Summary Statement 14.

A. (Perusing.)

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Q. You talked about evidence of smokers-related lung changes and in parentheses you have "smoker's macrophages and respiratory bronchiolitis"; is that right?

A. Right.

Q. Let's talk about smoker's macrophages first. Is your opinion on causation in this case depending upon the finding of smoker's macrophages?

A. Not really.

Q. Why not?

A. The most important thing is his history of smoking. The smoking macrophages is just to provide evidence that he's a smoker.

Q. Smoker's macrophages don't cause lung cancer, do they?

A. They don't.

Q. Lung cancer doesn't develop out of smoker's macrophages, does it?

A. It does not.

Q. Smoker's macrophages are not necessary or sufficient for lung cancer, are they?

A. No. That's correct.

Q. Now, if you can turn back to Exhibit 9 for me. It's the pathology report from March '96 after the chemotherapy and radiation therapy, correct?

A. Right, No. 9. After he was deemed to be a

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surgical candidate, yes.

Q. The pathologists who viewed the tissue at that time -- and I guess they were Drs. Carico, C-a-r-i-c-o, and Smith. I think it's the third page of that report. They noted non-neoplastic lung shows acute hemorrhage. Do you see that?

A. I see that, yes.

Q. When they describe a non-neoplastic lung in their report, they were talking about the same part of the lung you described as sections of lung parenchyma uninvolved by tumor in your report; is that fair?

A. I think it is, yes.

Q. In their original pathology report, Drs. Carico and Smith didn't describe smoker's macrophages, did they?

A. They did not.

Q. They described acute hemorrhage, right?

A. They did.

Q. Hemorrhage of the type that they described is consistent with the patient who just finished radiation and chemotherapy, isn't it?

A. Highly unlikely.

Q. You say it's highly unlikely?

A. Yes.

Q. Why is that?

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A. Because radiation activates sclerosis of the blood vessels and makes the lung be vascular, and chemotherapy causes more fibrosis and reactive changes. The most common cause of hemorrhage in people that have lung surgery is the surgery itself. If it was really caused by the radiation therapy and chemotherapy, what you'd be looking for is hemosiderin.

Q. Do you agree that chemotherapy can cause diffuse alveolar damage?

A. Yes.

Q. The initial phase of damage caused by chemotherapy can manifest as pulmonary edema and hemorrhage?

A. You can't say yes to that. The most common things that you see with chemotherapy, actually, is more of an interstitial edema and the reactive changes in the alveolar lining cells, and then you usually go into some pulmonary fibrosis.

Q. Can the body respond to alveolar damage caused by chemotherapy of alveolar macrophages?

A. Yes, it can. Sure. The difference between that, though, and smoker's macrophages is that smoker's macrophages are so characteristic. They have kind of a light tannish appearance, and they are present predominantly in the alveolar ducts, the alveoli, and the respiratory process.

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Q. Did you note which slides you saw that smoker's macrophages in?

A. Probably not, but I'll see if I did. (Perusing.) I guess I did in SP96-4435 F9.

Q. How long would you expect to see smoker's macrophages after someone has quit smoking?

A. It's been published in the literature as up to two years. What I've seen myself is several years.

Q. Under the microscope can you distinguish between smoker's macrophages and pollution-laden macrophages?

A. I think you can. Most of the time what you'd see, if I understand your word pollution macrophages, it's a macrophages that occurred in a person's lungs who is exposed to ambient air like a pollutant. Most of the time you have a black dust, whereas the smoker's macrophages have this tannish-brown hue to them.

I have some pictures of some here, but I'd have to show you one in a photograph that was colored to have you appreciate it.

Q. Now, we have been talking about smoker's macrophages and my assumption is -- you can correct me if I'm wrong -- that we are talking about smoking tobacco; is that correct?

A. It doesn't matter. Yes, it does. Smoking

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tobacco, right. It doesn't matter if it's cigarette smoking, pipe smoking. It's any type of smoking in which there is inhalation because approximately a third of the weight of the smoke actually is in the lung, so to speak; and in the form of a particulate matter that is deposited there and that usually goes by the macrophages.

Q. Let's try to clear that up because I know you have distinguished between tobacco and pipe and cigars.

Would a macrophages caused in someone who smokes marijuana appear differently than a macrophages caused by someone who smokes tobacco?

A. I don't know. I've not seen lungs from enough people who have smoked marijuana to know. I've seen very few lungs of people who have smoked marijuana that have not also smoked tobacco products.

The actual particulate matter that comes from the complexion of the tobacco also comes from the fact that the tobacco is contaminated with dust. That's not totally cleaned out when the cigarettes or cigars or whatever are made.

I don't know the answer to your question.

Q. It's also true that in marijuana smoking not all the dust or whatever that is that you described may be cleaned off the marijuana; is that --

A. I don't know. I don't know enough about how

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marijuana is actually processed.

Q. You don't know if you could distinguish under the microscope a macrophages caused by smoking cigarettes as opposed to smoking marijuana?

A. That's right. I don't know.

Q. So I can't rule out that the macrophages you observed in F9, I think you said, was caused by marijuana as opposed to cigarette smoke?

A. As I sit here today I can't, but I'm going to write myself a note to look at that and see if there's any literature on that. I couldn't, as I sit here today, tell you one way or the other.

Q. If you find any literature on that, I assume you will let Mr. Evans or someone at Ness, Motley know; is that right?

A. Sure.

MR. MURPHY: Jerry, I assume that you will let the defendants' know if you hear from Dr. Hammar with those results?

MR. EVANS: Yes.

(Request for production.)

Q. BY MR. MURPHY: Doctor, the second smokers-related lung changes that you described in your report is respiratory bronchiolitis, correct?

A. Correct.

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Q. Again, is your causation opinion dependent on the finding of respiratory bronchiolitis?

A. No.

Q. Respiratory bronchiolitis doesn't cause lung cancer?

A. No.

Q. Lung cancer doesn't arise from respiratory bronchiolitis, does it?

A. That's correct.

Q. Respiratory bronchiolitis is not necessary or sufficient for lung cancer?

A. That's correct.

Q. Now, I think you can tell from the pathology report, which we marked as Exhibit 9, that the tissue collected regarding that report was collected on March 11, 1996?

A. Yes.

Q. Let me back up a minute. Do you recall which slides you observed respiratory bronchiolitis on?

A. Probably on slides F9 and F10.

Q. Both of those are associated with the pathology report we marked as Exhibit 9, correct?

A. Yes.

Q. Again, that was collected on March 11, 1996?

A. It's a little bit confusing. They said the

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date collected was March 11, 1996; and they say date received is March 12, 1996. I don't know enough about how they do their pathology reports at that medical center. Most pathology reports would have the date received which would usually be the same day as the surgery, and then the date of the report that was transcribed and went out to the clinical doctor. I don't know if the date collected means that that's the day of the surgery or the day that they received the material in their lab. I don't understand that. I would have to get their clarification.

Q. In any event, it was somewhere in and around March 11 or 12, 1996?

A. Yes.

Q. I'm going to show you a record of January 29, 1996.

MR. MURPHY: Can you make this an exhibit, please?

(Defendants' Exhibit 14 was marked for identification.)

Q. BY MR. MURPHY: I'm going to hand you what we have marked as Exhibit 14 to your deposition. For the record it's one of Mr. Little's medical records dated 1/29/96. It's entitled "Ambulatory Care Pavilion," and it's got Bates Nos. 200409003-0078 and 0079.

Doctor, have you ever seen this record before?

A. No.

Q. I want to refer you briefly, I hope, to the

http://legacy.library.ucsf.edu/tid/udr07a00/pdf
Source: http://www.industrydocuments.ucsf.edu/tobacco/0001

second sentence under "Interval History."

A. Okay.

Q. See there it says, "The patient returns today in scheduled follow-up complaining of a cough, a temperature of 101 degrees, and a headache."

Do you see that?

A. I do.

Q. Now, that was one and a half months before pathology was collected in March, correct?

A. Approximately, yes.

Q. Directing your attention -- it's still on the first page -- to "Plan." Do you see that?

A. I do.

Q. The conversation there is, "After discussion (sic) the case with Dr. Stuart" -- the English is a little poor there, but it goes on to say, "we have decided to proceed with chemotherapy and place the patient on antibiotics with Amoxicillin." Do you see that?

A. I do.

Q. Amoxicillin is an antibiotic, correct?

A. Yes.

MR. MURPHY: I want this marked as next in line.

(Defendants' Exhibit 15 was marked for identification.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you what we have marked as Exhibit 15 to your deposition. I'll

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state for the record that it's one of Mr. Little's medical records dated 2/26/96, again entitled "Ambulatory Care Pavilion," with Bates Nos. 200409131-0077 to 0078.

Have you seen this record before?

A. No.

Q. I wanted to direct your attention to the third sentence under the section "Interval History." Are you with me?

A. I am.

Q. Is says, "The patient reports a dramatic improvement in his cough and sputum after taking Amoxicillin about three weeks ago." Do you see that?

A. I do.

Q. That refers back to the earlier record we saw, correct?

A. Yes.

Q. Mr. Little had taken the Amoxicillin and he now reports dramatic improvement, correct?

A. Yes.

Q. If a patient like Mr. Little had a temperature and a cough that was resolved by the antibiotic Amoxicillin, it's a good guess that the patient had a respiratory infection, is it not?

A. It is, yes.

Q. The symptoms that are described in these

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records are consistent with a recent pneumonia, couldn't they be?

A. Actually, yes.

MR. MURPHY: Let's have this marked as 16.

(Defendants' Exhibit 16 was marked for identification.)

Q. BY MR. MURPHY: I'm going to hand you what has been marked as Exhibit 16 to your deposition. For the record this is a chest x-ray report dated January 24, 1996. It's got Bates No. 200409016-0015.

Have you seen this before, Doctor?

A. No.

Q. I want to briefly refer you to, I think, the third sentence from the end of the paragraph under "Findings." Are you with me?

A. Under "Findings"?

Q. I guess I am going up from the bottom five lines or so.

A. Yes, I've got it.

Q. It says, "The appearance is certainly compatible with the history of bronchogenic carcinoma being treated and reduced in size or with resolving hematoma or a pneumonia adjacent to it."

Do you see that.

A. I do.

Q. So one of the potential diagnosis that this

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radiologist considered was a pneumonia in January of 1996, correct?

A. Yes.

Q. Do you know whether Mr. Little had a history of pneumonia prior to November of 1995 when the first -- or at least when the x-rays were taken that lead to his diagnosis of lung cancer?

A. I don't know.

Q. Now, would you agree with me that respiratory bronchiolitis is defined as an inflammation of the bronchials often associated with pneumonia?

A. Not the way pulmonary pathologists use respiratory bronchiolitis. It's a very distinctive lesion that's caused by cigarette smoking. If you wanted to use it in the overall context, what it could mean to anybody, the answer would be yes.

Respiratory bronchiolitis refers to a lesion in which the smoker's macrophages within respiratory bronchials and the alveolar ducts associated with slight thickening of the walls of those structures. If you were to just talk about respiratory bronchiolitis in a general sense, bronchiolitis does mean inflammation of airways, but that term really refers pathologically to a distinct cigarette smoking related lesion.

Q. And there's a distinction between respiratory

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bronchiolitis and smoker's macrophages in your understanding or how you use them?

A. They are part of the same thing. Respiratory bronchiolitis was actually observed in many young men who died in Korea. When they started doing autopsies on these people they found that many of their respiratory bronchials had thickened walls, and they had these macrophages in the respiratory bronchials and the alveolar ducts. This was determined to be smokers-related disease, and it still is.

Q. Now, Doctor, when you look at a cancer cell on a slide under a microscope, you can't tell what caused the cell to become cancerous, can you?

A. No.

Q. There isn't any staining that can be done that will tell you the cause of the cancer, is there?

A. No.

Q. And you can't look at a slide under a microscope and determine a patient's smoking history, can you?

A. No, not determine.

Q. Let me make the question more specific. You can't look at a cancer cell under a slide and determine a patient's smoking history, can you?

A. No.

Q. There's no staining that can be done to a

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cancer cell to determine if a patient was a cigarette smoker, is there?

A. No.

Q. Not only can you not tell whether the patient was a smoker but you can't tell how much they smoked or for how long they were a smoker, can you?

A. Not by looking at the cancer cells, no.

Q. What is your source of knowledge on Mr. Little's smoking history?

A. It was what was provided to me in the letter that I received from Mr. Patrick and also what was present in Dr. Harley's report.

Q. You have that letter from Mr. Patrick with you here today?

A. I do.

Q. Maybe over the lunch break we can take a look at what you brought with you, but at a minimum I think we could probably arrange to get a copy of that and I would like to get that.

A. Okay.

(Request for production.)

Q. BY MR. MURPHY: I want to ask you if you could switch back to, I think, Exhibit 3 which is your cover letter to Mr. Patrick.

A. Okay.

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Q. Do you have it there?

A. I do.

Q. Now, I want to read a little bit from the first paragraph. Starting with the third sentence you note there, "Dr. Harley detailed Mr. Little's medical history and indicated that he had smoked cigarettes from 1960 or 1961 to 1995. He started smoking about one park a day and worked up to smoking two packs a day. His total pack years was probably somewhere between 35 and 45."

Do you see that?

A. Yes.

Q. Am I right that you are attributing that information to coming from Dr. Harley?

A. Yes.

Q. The only information you had from Dr. Harley was his report; is that correct?

A. Yes, that's correct.

Q. Do you have Dr. Harley's report there? I think it's Exhibit 5.

A. Here it is right here.

Q. Can you turn to the second page of Dr. Harley's report?

A. Yes.

Q. Do you see where it says "Tobacco"?

A. Right.

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Q. Dr. Harley reports that Mr. Little smoked about a pack of cigarettes a day for about 25 years. Do you see that?

A. Right.

Q. That's different from what you attribute to Dr. Harley in your cover letter to Mr. Patrick in Exhibit 3, correct?

A. It looks like it is, yes. I'm trying to see if maybe it's my error. (Perusing.) I think that was actually information that came from Mr. Patrick's letter not Dr. Harley's report.

Q. You got a little bit ahead of me. I was just going to ask that question because in your report -- and it's really the first paragraph of your report -- you noted some information about Mr. Little's smoking history, and in your report you attributed it to coming from Mr. Patrick.

A. Right. That's my error.

Q. I'm not -- believe me, I'm not pointing it out to show you that you made a mistake. What I'm pointing it out for you to do is to get you to agree that that is information that you received from Mr. Patrick and the information in Dr. Harley's report are inconsistent, aren't they?

A. (Perusing.) They would not be totally consistent. That would be true, yes.

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Q. Do you recall what Dr. Roggli said about Mr. Little's smoking history?

A. Not off the top of my head, but I will look and see. (Perusing.)

Dr. Roggli said that he smoked one pack of cigarettes per day for 20 to 30 years, discontinuing smoking in November 1995.

Q. That's information that's not consistent with the information you received from Mr. Patrick; is that correct?

A. It is not precisely the same, no.

Q. Neither Dr. Roggli or Dr. Harley ever indicated that Mr. Little smoked more than a pack a day, did they?

A. I think if you read Mr. Patrick's letter, he kind of goes out of his way to talk about the correct smoking history.

Q. You are getting a little bit beyond my question, but I don't want to cut you off.

A. No, that's okay. You can add that in, but I just want to make sure I get an answer.

I said no. No.

Q. My next question was: Neither Dr. Harley nor Dr. Roggli report a pack year smoking history of between 35 to 45 years, do they?

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A. No, they do not.

Q. I really didn't mean to cut you off from talking about Mr. Patrick's letter. My plan is to review that over lunch and possibly talk about it afterwards.

A. You have every right to cut me off. Any time you want to, that's fine.

Q. I hate to do that, and I hate when people do it to me. If you have any comments about that, I want to make sure you get them in if you need to.

You never went through the medical records yourself to determine what they said about Mr. Little's smoking history, did you?

A. No.

Q. Now, if you were reviewing a patient's medical records to try to make a determination of what their smoking history was, if there was conflicting information about that smoking history so that the information in the records, before litigation involving the patient's smoking was filed, indicated a lesser history than information in the records from after the litigation involving the patient's smoking history was instituted, would you view those records -- that is, the pre- and post-litigation records -- differently?

A. I'm not sure exactly how to answer that. I don't think I can answer that in a yes or no answer. I think that what you find in reality in most medical records

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is that there's often disparities in smoking histories.

With respect to which is correct, it probably could depend on the exact setting. I don't know. I guess there's often, perhaps, no way to absolutely prove what is the correct history one way or the other.

I guess if there was something said differently after litigation was instituted that gave a higher smoking history, then one might assume that was incorrect; but on the other hand, you can get up to a certain number of pack years and I'm not sure that it makes a whole heck of a lot of difference.

Q. Let me ask this as a hypothetical.

A. Okay.

Q. A smoker told his doctors that he smoked one pack per day or less pre-litigation involving his smoking then post-litigation the same smoker told his doctors he had over his history smoked two packs per day.

Which would you consider more reliable, the one pack per day or the two packs per day?

A. What I have seen frequently myself is that most people don't like to admit to their doctors they are smokers, so I would actually trust the second history the most. That's because when doctors ask people who have lung cancer how much they smoke, they don't give usually the correct amount. They under estimate.

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Q. Have you ever had a case where you had a patient who was involved in litigation over their smoking who told you different amounts or gave you a different smoking history pre- and post-litigation?

A. Not that I have seen myself. I have seen medical records where you could find, I would say, a variation of as much as three-fold in a person's smoking history. In the asbestos cases it's usually the opposite way. It seems like there is a underestimate about what the person sometimes talks about versus what is presently in their charts.

In the medical records I have seen, I would say the majority of them are people who report smoking, but when doctors report what people say about their smoking histories there often is variation from one record to another.

Q. Wouldn't you agree, though, that in the hypothetical that I have presented that involves litigation, that the smoker had the incentive to exaggerate his smoking history?

MR. EVANS: I'll object to the form.

MR. MURPHY: Doctor, you probably know from your prior depositions that you can still answer.

A. I would say that I think that's probably true, yes.

MR. MURPHY: This is a good time for a break for me

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if it fits you all.

MR. EVANS: That's fine.

MR. MURPHY: Off the record.

(Luncheon recess was taken.)

(Defendants' Exhibits 17 & 18 marked for identification.)

Q. BY MR. MURPHY: Doctor, we are back on the record after lunch.

A. Okay.

Q. Before we started we had a discussion over how we can attach your file of the Little case to the deposition as an exhibit, and we've agreed to mark your file as Exhibit 17; is that right?

A. Yes.

Q. And the court reporter is going to take that with her, and she will get your originals back after she makes them for the depositions; is that okay?

A. Yes.

Q. We made at least two alterations to your file. One is, you have taken the photomicrographs out so that you can make those duplicates yourself, and you'll get those to us. We talked about that this morning, right?

A. Yes.

Q. The second thing is we have taken out the letter from Charles Patrick to you, dated February 17, 2000, and we've marked that separately as Exhibit 18; is that

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right?

A. Yes.

Q. And hopefully on a break we will be able to make a copy of that, so we are sure you have all your materials, all right?

A. Fine.

MR. MURPHY: Counsel, just for the record, after Exhibit 18 was handed to me, I noticed that there is a legend at the top, "attorney work product, privileged and confidential."

I alerted you to that, and you've agreed that we can see that and use that in this deposition in this case; is that correct?

MR. EVANS: Yes. I'm going to let you refer to this during this deposition.

Q. BY MR. MURPHY: Doctor, while we have Exhibit 18 in front of you, that's the letter from Charles Patrick?

A. Yes.

Q. Did you review that letter in preparing and formulating your opinions in this case?

A. Yes.

Q. Are your opinions based on information contained in the letter from Mr. Patrick?

A. Some are, yes. Primarily the smoking history.

Q. Let me go back and ask a question about the

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photomicrographs. I think this may be cleared up on the record but...

You need a projector to read those slides?

A. To see them, you know, more easily, yes.

Q. And you sit here today there is really no reasonable way for us to talk about what is depicted in any of those, is there?

A. (Perusing.) You know, I guess it would be easy enough for me to tell you what these all are. That would be very simple; but for me to point out what each one shows, it would be easier to do it with a projector.

Q. Do you intend to show the jury the slides that you took?

A. It would kind of depend on what the issues are and whether or not certain issues came up or certain statements were made with respect to what type of cancer Mr. Little has.

Q. Is it possible to make prints from those slides that we would be able to see?

A. Yes, very easy. I mean, very easy but relatively expensive depending on what size prints you want to make.

Q. Did plaintiff's counsel ask you to make any prints before the deposition today?

A. No.

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Q. Is it fair to say that at this time you would be unable to answer questions about specific features shown on each slide because we don't have a print or a projector here today?

A. I actually think I can tell you exactly what is present on every slide, but I'm not sure that it would be necessarily worth your time to do that.

Q. Because it's a slide and there is no way for us to look at an enlarged picture, would you be able to describe for me so that I could see where you saw, let's say, the prickles that would demonstrate a squamous cell carcinoma?

A. That might be pretty hard to see on these slides, yes. It would be easier with a projector. It would always be easier to look at them through a projector or have the prints made up to see them.

Q. Doctor, do I understand correctly that you keep a file somewhere of articles related to alcohol consumption and cancer?

A. Yes.

Q. If we needed it for the purposes of this case, would it be possible for us to get a copy of that file?

A. Yes.

(Request for production.)

Q. BY MR. MURPHY: You would agree that alcohol

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consumption has been shown to be a causal factor in certain cancers?

A. I agree with that statement in general on certain cancers, yes.

Q. You have not made a systematic study of the literature on the relationship of alcohol consumption and lung cancer, have you?

A. I've looked at a lot of articles on that issue. As far as every one, no. As far as a significant number, yes.

Q. And I'm trying to break down some testimony of yours in the past in a short-circuited way, and maybe I'm missing something.

My understanding is that you review several journals, and to the extent that a journal you ordinarily review has an article about the relationship between alcohol consumption and lung cancer or other cancers, you would review such an article; is that fair?

A. That is fair.

Q. My understanding was, also, that you haven't, let's say, done a MEDLINE search or gone to the library and in other ways specifically tried to accumulate articles that have researched the relationship between alcohol consumption and lung cancer; is that fair?

A. That's not fair. Actually, I have done that.

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I've done that for the Gilboy case, and I actually did that for the Whiteley case.

Q. That research would be contained in your file?

A. It may or may not be in the file. It would be in the articles I have reviewed. A lot of the articles I have are ones to file, but hopefully I should be able to put my hands on that.

The other thing, I have done MEDLINE searches on that issue on more than one occasion. I have a significant number of articles. Not everyone has been published. Sometimes I have just obtained review articles.

Q. You haven't done any firsthand research on the relationship between alcohol consumption and lung cancer have you?

A. No.

Q. When you look at a cancer cell on a pathology slide, you can't tell from that observation whether alcohol was involved in causation of cancer, can you?

A. No.

Q. There's no staining that you can do that would provide that information, is there?

A. No.

Q.

[DELETED - PERSONAL INFORMATION]

A.

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Q.

A.

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Q.

A.

Q.

A.

Q. I also understand that you keep a file on

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articles that discuss the relationship between marijuana smoking and lung cancer; is that correct?

A. Yes.

Q. I'll try to get the same questions out as I did with alcohol.

Are the articles included in that file based on a systematic review of the research that you have done?

A. They were articles that I obtained from a MEDLINE search, and I did not obtain every article that was mentioned. I usually would obtain review articles that would usually refer to most of the critical studies that had been published in the past.

Q. You haven't done any original studies on the relationship between marijuana smoking and lung cancer, have you?

A. Actually, I was involved in a task force one time many years ago where we were specifically trying to determine what the risk was of lung cancer to people who smoked marijuana. We met several times and finally came to the conclusion that there was not enough data to make any determination at that point in time, and that group disbanded. That's the only kind of a semi-official group I was involved with.

Q. So just let me try to summarize. Your group was not able to conclude one way or another whether

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marijuana smoking caused lung cancer; is that right?

A. That is correct. That group was actually formed by the Washington State Society of Respiratory Disease. They're the affiliate of the American Thoracic Society.

Q. When you look at a cancer cell on a pathological slide, you can't tell from that observation whether marijuana was involved in causation of that cancer, could you?

A. No.

Q. And there's no staining you can do that would provide that information, is there?

A. No.

Q.

A.

Q.

[DELETED - PERSONAL INFORMATION]

A.

Q.

A.

Q. Do you have -- strike that and I'll start with a new one.

In your book you mention some dietary factors that may

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play a role in the causation of lung cancer; is that right?

A. Yes.

Q. You can't look at a cancer cell on a pathology slide and determine whether or not those dietary factors played a role in the development of that particular cancer, can you?

A. No.

Q. And there is no staining you can do that would provide information on that, is there?

A. No.

Q. Do you have any information on what Mr. Little's diet was?

A. No.

Q. Asbestos causes lung cancer, correct?

A. Yes.

Q. Does asbestos also cause pleural thickening?

A. Yes.

Q. Is there anything else that can cause pleural thickening?

A. All kinds of things.

Q. Smoking doesn't cause pleural thickening, though?

A. It actually does cause pleural thickening. Specifically, when you get emphysema in the upper lobes, it's very common for there to be significant visceral

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pleural thickening. It's not infrequent to get focal adhesions between the visceral and parietal pleura caused by smoking-related emphysema.

Q. Mr. Little did not have emphysema, did he?

A. Not that I'm aware of, no.

Q. Are you aware of any pulmonary function testing that was done on Mr. Little at any time?

A. (Perusing.) No.

Q. Now, when you look at cancerous cells under a microscope, there's nothing about that observation that could tell you asbestos exposure was involved in the causation of that cancer, is there?

A. No.

Q. There is no staining you can do to those cancerous cells to determine if asbestos was involved in the cause, is there?

A. No.

Q. Do you have any knowledge regarding potential asbestos exposure by Mr. Little?

A. (Perusing.) Not that I can recall. Maybe I could look briefly through that letter from Mr. Patrick.

Q. Do you still have it over there?

A. No. You didn't give it back to me.

Q. I thought I did. It might be -- if you close the file, it's on the other side.

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A. There we go. Okay. Thank you. (Perusing.) No, I do not.

MR. MURPHY: Why don't you just mark this next in order.

(Defendants' Exhibit 19 was marked for identification.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you what's been marked as Exhibit 19 to your deposition. For the record, this is a report of a chest x-ray, dated December 6, 1995, and it's got Bates No. 200409098-0006.

Have you seen this radiology report before today?

A. No.

Q. I want to direct your attention, if I can, to something in the paragraph after "Findings." I guess what I'm looking at is the sentence that starts four lines from the bottom. See there where it says, "A small amount of pleural thickening is seen at the left apex which is under the mass"?

A. Yes.

Q. Do you see that?

A. Yes, I do.

Q. I take it you have not made any determination of what the cause of that pleural thickening that was seen in Mr. Little's chest x-ray was, have you?

A. (Perusing.) No.

Q. Doctor, radon can cause lung cancer, correct?

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A. I think that is a highly debatable issue right now, and I don't have any answer for that. It turned out that most of the people who have been exposed to radon who developed lung cancer were cigarette smokers. As far as I know -- and I guess attorneys would say it's hearsay evidence -- it does not, based on a friend of mine who works at the National Cancer Institute who does epidemiologic research.

Q. Who is that friend?

A. Her name is Lois Travis. It's Bill Travis' wife.

Q. You would be relying on Dr. Travis to support any opinion that radon doesn't cause lung cancer?

A. I wouldn't do that. I would actually have to do a current MEDLINE search.

It's my understanding from when I've talked to Lois Travis and talked to Bill Travis about radon and lung cancer is that there is very little information or very little evidence at this point in time that radon causes lung cancer. The majority of people who developed lung cancer erratically related to radon have also been cigarette smokers who have had a significant smoking history.

I don't have that written down someplace as something that I could prove to you, but that's what I've been told.

Q. You did research on radon and it's

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relationship to lung cancer in order to do your book, correct?

A. Many, many years ago I did, yes.

Q. You would want to update that research before you made an opinion?

A. Yes. I did update partially in the second edition. I indicated in there that there was a lot of controversy about radon and lung cancer, but enough years have gone by since that book was published to update it again so I wouldn't want to say much about that until I did some further research.

Q. When you look at a cancerous cell under the microscope, you can't tell whether or not radon was involved in the causation of that cancer, can you?

A. No.

Q. There's no staining that would show or would allow you to exclude radon as a cause of the cancer, is there?

A. No.

Q. Diesel exhaust exposure has been associated with lung cancer?

A. Yes.

Q. There is no way you can determine from observing a cancerous cell under a microscope whether diesel exhaust had a role in the development of that cancer, is

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there?

A. No.

Q. There is no staining you could do that would provide information on that subject?

A. No.

Q. Do you have any information on Mr. Little's exposure to diesel exhaust?

A. No.

Q. Do you have any information on Mr. Little's exposure to radon?

A. No.

Q. The book lists certain occupational exposures that have been associated with the development of lung cancer; is that right?

A. Yes.

Q. You list nickel as one of those exposures?

A. Yes.

Q. Exposure to copper as being associated with lung cancer?

A. Yes.

Q. Exposure to beryllium as being associated with lung cancer?

A. Yes.

Q. Exposure to arsenic?

A. Yes.

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Q. Exposure to chromate?
A. Yes.
Q. Exposure to chloromethanal ether?
A. Yes.
Q. Exposure to vinyl chloride?
A. Yes.
Q. Exposure to benzene?
A. Yes.
Q. There is no way you can look at a cancerous cell under the microscope and determine whether any of those occupational exposures played any role in the development of a person's lung cancer, is there?
A. No.
Q. There is no way that you could do that that could provide me with any of that information, is there?
A. No.
Q. Do you have any knowledge regarding Mr. Little's exposure to any of those occupational exposures?
A. No.
Q. Now, in your book you also talked about genetic factors as playing a role in the development of lung cancer; is that right?
A. Yes.
Q. You can't look at a cancerous cell under a

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microscope and tell whether genetic factors played a role in the development of a person's cancer, can you?

A. No.

Q. You can't even tell if a person had a genetic susceptibility to cancer by looking at a cancerous cell under a microscope, could you?

A. No.

Q. Do you have any knowledge regarding Mr. Little's family history of cancer, generally?

A. No.

Q. Do you have any knowledge regarding the history of lung cancer in Mr. Little's family?

A. No.

Q. Doctor, hopefully I can do this in a way that we can sum it up fairly quickly.

When you look at a cancerous cell under a microscope, you can't tell from that what a person's history of alcohol consumption was, can you?

A. No.

Q. You can't tell what their history of marijuana smoking was, can you?

A. No.

Q. You can't tell what their diet was, can you?

A. No.

Q. You can't tell what their history of asbestos

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exposure was, can you?

A. No.

Q. You can't tell what their history of radon exposure was, can you?

A. No.

Q. You can't tell what their history of diesel exhaust exposure was, can you?

A. No.

Q. You can't tell what their history of occupational exposures was, can you?

A. No.

Q. Your book also talks about the potential role of viruses in the development of lung cancer?

A. Yes.

Q. When you look at a cancerous cell under a microscope, you can't tell if a virus played any role in the development of lung cancer, can you?

A. No.

Q. Your book also notes that there were certain unknown causes that appear to be operative in the development of lung cancer; is that fair to say?

A. There are cases where you can't determine the cause.

Q. When you look at a cell under a microscope, you can't tell if unknown causes played a role in the

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development of that cancer, can you?

A. No.

Q. Now, at the start of our deposition you mentioned a case or cases in litigation where you could not come to the conclusion that the cancer in the person involved was caused by their cigarette smoking, and I think you said one of the reasons was that they had a low number of pack years of smoking; do you recall that?

A. Yes.

Q. When you talk about exposure to asbestos and some of the diseases that asbestos can cause you hear talk of a threshold level exposure necessary to cause disease; is that right?

A. Yes.

Q. Is there a threshold or minimum threshold level of cigarette smoking necessary to cause lung cancer?

A. I don't know. I'd have to look that up. Obviously, there's a very strong association between the incidence of lung cancer and the number of pack years smoked.

Is there a threshold before which lung cancer does not show an increase in smokers? I would have to look that up. I think there is for people who are exposed to asbestos.

Q. Now, it seems to me that when we talked about this at the beginning of the deposition, in a person who

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apparently had a low number of pack-year history of cigarette smoking, you could not come to the conclusion that that that person's cancer was caused by their cigarette smoking.

Is there a certain number of pack years below which you would not conclude that a person who smoked for that long and developed lung cancer that their cancer was not caused by smoking?

A. I don't think I can answer that yes or no, but I think I can explain to you what I meant. I've seen cases in asbestos litigation where people who have smoked maybe as few as a few months or maybe one or two years at a very low rate, and it may be 40 or 50 years before they are diagnosed with lung cancer, and it's very hard for me to relate that lung cancer to cigarette smoking.

I have never gone, actually, and thoroughly reviewed the literature on if there is any data of a threshold. I've done it very extensively on asbestos but not for cigarette smoking. I would have to do that before I could answer that question.

Those are the type of cases I'm talking about. People that smoke just a minimal amount many, many years before they got lung cancer frequently, particularly in persons who have the disease asbestosis.

Q. You have heard the toxicological maxim that

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the poison is in the dose?

A. Sure.

Q. Doctor, even with regard to substances that are known to cause disease, typically there's a minimum level of exposure that one must achieve before you can say that their disease was caused by that substance.

A. That's true. Most carcinogens have a dose response relationship just like asbestos and cigarette smoke. I think that's true. What I don't know with respect to cigarette smoke is what is the lowest level at which you see a significant increased incidence of lung cancer. I would have to research that. I don't know.

Q. I know we talked about this to some extent already but just for clarity, am I right that Mr. Little's lung cancer did not arise in a major airway?

A. I'd say major airway, if you define a major airway, say, as greater than a centimeter in diameter.

Q. You would agree with me that it didn't arise in a major airway?

A. As far as I can tell from the pathology report, that would be correct.

Q. Your opinion is consistent with the way you would define major airway; is that right?

A. Well, I guess if you define it as something greater than a centimeter in diameter, yes. But I'm not

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sure that's how you define it. Assuming that that is the definition.

Q. You just don't know how you'd define a major airway?

A. Well, major airway is somewhat of an ambiguous term because all airways in some respects are pretty important. I guess the ones that are the largest and provide the air to both lungs are perhaps most important, but obviously the ones that provide it to the lobes are important. I don't know at what point you stop considering something a major airway and say it's a minor airway. I don't know what the definition of that is. Maybe there is a definition, but I don't know it.

MR. MURPHY: Let's mark this as next in order.

(Defendants' Exhibit 20 was marked for identification.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you what's been marked as Exhibit 20 to your deposition. I'll tell you that this is a chart we prepared on cell types of lung cancer, and I'm going to ask you some questions about it.

A. All right. Sure.

Q. Does this chart correctly indicate the four major cells types of lung cancer?

A. It is fine. I don't have any big disagreement. The only thing I would say is that you can

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have mucous secreting acinar type adenocarcinomas, and you can have as indicated you can have mucinous producing bronchioloalveolar cell carcinomas. I just don't know if I would put a mucous secreting as a major subtitle. I think that's just a thing that many adenocarcinomas do -- mainly, about 75 percent of them.

I think these other types -- the acinar type -- is a pretty distinct type, the papillary is a distinct type, and the bronchioloalveolar cell type as long as you understand what that is.

Q. You would consider bronchioloalveolar as a subset of adenocarcinoma as we talked about?

A. I would, yes.

Q. And you agree with me, in any event, on the four major subtypes of lung cancer that are listed one through four there?

A. I do. Like I said, with that exception of that mucous. The four major types of, yes. I agree with that, yes.

Q. Let's talk for a few minutes, if we can, about large cell carcinoma. I know we made some comments about it this morning, but you referred to large cell as a wastebasket category, correct?

A. It is kind of a wastebasket category because basically it's a tumor that is composed of cells that are

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perceived to be large that show no other type of differentiation. By that I mean, they don't show granular differentiation and they don't show squamous differentiation and they don't show neuroendocrine differentiation.

When all is said and done, when you look at them in various ways, they all actually show some type of differentiation. It's just that you can't see it by light microscopy.

Q. Would you consider the category for the diagnosis of a large cell carcinoma to be a diagnosis of exclusion?

A. It basically is a diagnosis of exclusion, and it kind of depends on how many tests you want to do to try to put it into another category. It is somewhat of a diagnosis exclusion, although it's very well defined as a distinct entity.

Q. Would you agree with me that large cell carcinomas tend to be peripheral?

A. I think those can be anyplace they want to in the lung. I don't think there's any absolute location for a large cell carcinoma. I think they often are peripheral. I would say that they are more commonly peripheral than they are central as far as being around a major airway of some kind.

Q. More times than not large cell carcinomas

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would be peripheral?

A. I would say that's true.

Q. Now, have you ever undertaken to study literature in assessing the relationship between large cell carcinoma and cigarette smoking?

A. I don't know if I've specifically done an assessment of that association or not. The place where I did do that type of assessment was when I was involved from 1977 to 1989 as the chairman of the pathology section of the lung cancer study group. It was our job to classify and anatomically grade all tumors that went into various study sections of people that were being treated. I kind of have a good feeling with what we found in that group with respect to what was observed with respect to cigarette smoking habits and the histologic type of lung cancer.

Q. Did you publish any of the research from that work?

A. It was published in all kind of articles mainly having to do with treatment. It was not published from a pathology point of view.

Q. Did any of publication regarding that work deal with the relationship between cigarette smoking and large cell carcinoma?

A. Not specifically that distinct association, no.

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Q. Would you agree with me that there is a weaker association between cigarette smoking and large cell carcinoma than there is for squamous or small cell?

A. I would agree with you, yes.

Q. Now, already we have mentioned the concept of dose response, correct?

A. Yes.

Q. When you are studying the relationship between an agent and a disease, it's important to identify a dose response relationship, isn't it, in order to determine the relationship to be one of cause?

A. I think that is an issue when you're talking about carcinogens causing cancer in general. I think you always have the other issue that there can be a very large range over what's considered carcinogen causes and a given type of cancer. But I think that is an important thing to evaluate.

Q. Do you know of any literature that's found a dose response relationship between cigarette smoking and large cell carcinoma?

A. I don't know if I have seen any articles that have specifically looked at that or not that I can remember. I know I have articles that have given a percentages of people who have large cell carcinoma who are cigarette smokers, but I don't know if I've seen articles that

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specifically talk about a threshold or a dose response type of interaction or study.

Q. Let me shift gears and ask you at least one question about squamous cell carcinoma.

It's true that in cigarette smokers all squamous cell cancers occur centrally, isn't it?

A. Yes.

Q. Back up a minute because I think I jumped ahead of myself and wasn't finished with my questions on large cell.

You've stated in your book that when you look at large cell cancers using electron microscopy it might be possible to make a different diagnosis of cancer; is that right?

A. Yes.

Q. What you found is that in 80 percent of cases the cancer diagnosed as large cell, after evaluation using electron microscopy, it turns out that those are adenocarcinomas; is that right?

A. That's right.

Q. You found that in 10 percent of the cases electron microscopy will show that those cancers are squamous cells?

A. Right.

Q. You did not review any of the pathology in this case under the electron microscope?

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A. I did not. That is true.

Q. Adenosquamous is a rare form of lung cancer, correct?

A. It is.

Q. The chart that I listed the major cell types on doesn't have adenosquamous on it; is that right?

A. It does not.

Q. The chart would be correct because adenosquamous is not a major cell type; is that right?

A. It is not a major cell type. That is correct.

Q. I think the percentages in your book for adenosquamous accounts for .4 percent to 4.0 percent of lung cancers?

A. Right. That's based on published literature, yes.

Q. That's between 1 and 25 lung cancers and 1 in 250 lung cancers are adenosquamous; is that right?

A. Fair enough.

Q. Adenosquamous cancers usually occur in the periphery?

A. They do.

Q. There is frequently early metastasis in adenosquamous cancers?

A. It's been studying to be more of a form of cancer than adenocarcinoma by itself or adenosquamous by

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itself.

Q. Let's talk for a minute about adenocarcinoma. That's a type of lung cancer least associated with cigarette smoking, correct?

A. Correct.

Q. It's the most common form of lung cancer among non-smokers?

A. Correct.

Q. Most adenocarcinomas arise in the periphery?

A. Right.

Q. We talked about the new WHO classifications, but they still list BAC as a subtype of adenocarcinoma?

A. Yes.

Q. And you agree with that classification?

A. Yes.

Q. Because you were part of it; isn't that true?

A. Yes.

Q. You noted in your book that adenocarcinomas are increasing in frequency; is that correct?

A. Yes.

Q. Your book also notes that the majority of pulmonary adenocarcinomas are associated with scarring?

A. Yes.

Q. And that's correct, isn't it?

A. Yes, it is. That doesn't mean they arise from

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scars or associated with scars.

Q. We'll talk a little bit more about that.

I wonder if you could find Dr. Harley's report for me for a minute?

A. Okay. (Perusing.)

Q. Can you turn to the last page of Dr. Harley's report?

A. Yes.

Q. The last two sentences of the paragraph that runs over from the prior page read: "However, some" -- and I think what Dr. Harley is referring to by some is lung cancers -- "arise from the airsacs (alveoli) and small airways. These are called bronchioloalveolar cancers and are often not associated with smoking."

Do you see that?

A. I do.

Q. Do you agree that bronchioloalveolar cancers are often not associated with smoking?

A. No.

Q. You would disagree with Dr. Harley on that subject?

A. I would.

Q. When you say you disagree with Dr. Harley regarding whether BACs are associated with smoking, what classification or criteria for diagnosis of BAC are you

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using?

A. I'm basically using the WHO classification that's written in this book or written in previous WHO classifications, which is basically a peripheral type of lung tumor that usually occurs solitary although maybe multi-focal and usually occurs or arises from cells that show either Clara cell differentiation on differentiation, from Type 2 pneumocyte differentiation. They tend to spread or grow along preexisting alveolar septa. They show both a mucinous and nonmucinous type of histologic pattern.

Q. Is it your testimony or opinion that a BAC that meets that definition is associated with cigarette smoking?

A. I believe it is. In the majority of cases I've seen in my practice as a pathologist it occurred in cigarette smokers. There are some publications back in the 50s of women with BACs, but the majority have not been cigarette smokers. There's a great deal of information right now on precursor lesions to this type of tumors; specifically, what's called atypical adenomas, hyperplasia of the lung.

At least in two of the largest studies, every person in the group who had been identified to have that precursor lesion had been a cigarette smoker. There is some suggestion that the carcinogens in cigarette smoke cause

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that type of change and that that may be the primary reason that we're seeing an increase in the incidence of adenocarcinoma in the lung at this point in time.

Q. In your book you had made a reference to a study by Auerbach and Garfinkel on BAC and the relationship, if any, between BAC and lung cancer; do you recall?

A. Vaguely, yes.

Q. In the text that I have it's on page 1143.

A. Okay.

Q. In the section of the book that goes from pages 1142 to 1143, you talk about an Auerbach and Garfinkel study of 505 cases of lung carcinoma. Do you see that?

A. Is that under the section of BAC or just in general about lung cancer?

Q. The section is called "Changes and Variations in the Histologic Subtypes of Lung Cancer."

A. I've got that now.

Q. You did the same thing I did, turned to the BAC section.

Do you see the reference to Auerbach and Garfinkel, the second from the last paragraph before the section that starts, "lung tumor heterogeneity."

A. I've got you.

Q. Do you see where it mentions their study and it goes on to note that the incidence of bronchioloalveolar

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cell carcinoma more than doubled in the two time periods that they had studied?

A. Right.

Q. And that they believe that these changes in incidence resulted from decreased lung cancer related to cigarette smoking and raised the possibility that the other etiologies may be important in the development of some lung neoplasms. Do you see that?

A. I do.

Q. What Auerbach and Garfinkel were saying was that they did not believe that BAC was related to cigarette smoke; do you recall that?

A. That's what they said, yes.

Q. And you disagree with Auerbach and Garfinkel?

A. I think that all those people are cigarette smokers. That's my understanding.

MR. MURPHY: May I have this marked as the next one?

(Defendants' Exhibit 21 was marked for identification.)

Q. BY MR. MURPHY: Doctor, do you rely on any particular published studies in your opinion that BAC is related to cigarette smoking?

A. I would have to go back to my papers. I have a lot of the papers on BAC, and I'd pick out which ones I relied on. I think there's going to be varying percentages

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of people who are smokers and nonsmokers and people who have adenocarcinoma in general, including BAC.

My observations have been while I've been working in Bremerton that we have a very high incidence of lung cancers. Over 90 percent of the people that have that type of cancer have been cigarette smokers. And that's also been my observation when I worked for the Pathology Reference Center in the lung cancer study group. Over 90 percent of the people that developed that type of cancer were smokers.

Q. Have you done any studies or scientific analysis based on your observations that you just described in your practice?

A. Have I done any? I've not published that. I've not done any statistics on that. It's just an observation I have made.

The reason I make that observation is that I'm the head of the cancer committee in our hospital in Bremerton, and I do this annual report every year where I look at various types of cancer, incidences of cancer, what causes the cancer, et cetera, et cetera. I've just completed a new study -- almost completed a study -- where we looked at cancer over ten years in Bremerton, specifically because we're writing this paper on a rare type of primary lung cancer called pseudomesotheliomatous adenocarcinoma of the lungs. We wanted to find out how frequently that occurred

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in Bremerton, and as a result of that we got a very good idea of how many people in Bremerton who developed cancer were smokers versus non-smokers.

BY MR. MURPHY: We've been going over an hour. This is probably a good time for a short break.

(Recess taken.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you what has been marked as Exhibit 21 to your deposition and ask you if you have seen that article before?

A. I have not, no.

Q. Doctor, for the record, Exhibit 21 is an article entitled "Bronchioloalveolar Carcinoma," by John Barkley and Mark Green; is that right?

A. Yes.

Q. It's published in the Journal of Clinical Oncology. Do you see that?

A. I do.

Q. It's from 1996?

A. Yes.

Q. I take it you don't regularly receive the Journal of Clinical Oncology?

A. I do not, no.

Q. Now, I want to ask you a couple of questions about Dr. Barkley's and Dr. Green's article. First, I want to ask about some statements in the results section which is

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on the first page in the abstract?

A. All right.

Q. It's the second sentence there. It says, "Patients with BAC tend to be younger at diagnosis, are more likely to be female, and less likely to be cigarette smokers when compared with other patients with non-small-cell lung cancer."

Do you see that?

A. I do.

Q. Do you agree with that statement?

A. (Perusing.) I guess before I can answer that question I'd have to learn a little bit more about some of the definitions that conclusion is based on it. I'd be happy to do that if you want me to. If you don't want me to do that, all I can say is that I can't say one way or the other. My own experience has been that I haven't seen that.

Q. Maybe what I should do is break it down so we are clear because the sentence, as it's written, contained about three elements.

Do you agree that patients with BAC are likely to be younger than those with other cell types?

A. Not necessarily, no. Now from what I've seen myself.

Q. Do you agree that patients with BAC are more likely to be female?

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A. Not from what I've seen myself, but I think that's partly one of the problems -- exactly how BAC is defined. If you go by this current edition of this book, there are very few pure BACs. In fact, most adenocarcinomas of the lung show a variety of different histologic patterns. It's very uncommon to see a pure BAC. It does exist, and I guess the ones I think are the purest would be the mucinous type that would be multi-focal or even a nonmucinous type that would a pneumonic type of form.

Q. Maybe we should start with the criteria that these authors use for diagnosing BAC. Let me make sure you understand that this is a review article.

A. I understand that, sure.

Q. You understand that these authors didn't actually do the pathology and make the diagnosis of BAC?

A. I understand that, also.

Q. What they have done here is review the literature and come up with some conclusions based on the literature. Do you see that?

A. I do understand that.

Q. They do have a table on page 2379 of their article that contains a diagnostic criteria for BAC. Do you see that?

A. I do.

Q. Do you agree that no evidence of extrathoracic

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primary adenocarcinomas is one of the diagnostic criteria for BAC?

A. Yes.

Q. Do you agree that absence of central bronchogenic source is another diagnostic criteria for BAC?

A. Yes.

Q. Do you agree that a peripheral parenchymal location is diagnostic criteria for BAC?

A. Yes.

Q. Do you agree that no distortion of pulmonary interstitium is another diagnostic criteria for BAC?

A. I think this book allows some distortion, but I would say not a great deal of distortion.

Q. By "this book," you are talking about the new WHO classification scheme?

A. Yes.

Q. They would allow some distortion?

A. There can be some cases of mild interstitial thickening from BAC, yes.

Q. So the definition, at least as it's written in the new WHO book, might be a little broader than --

A. Maybe a little broader, but it's also maybe a lot more less broad, actually. That's actually fine. I don't disagree with that.

Q. The fifth criteria they have is neoplastic

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cells growing along alveolar septae. Do you agree that that's a diagnostic criteria?

A. I do.

Q. Would you add to this criteria listed on Table 1, the diagnostic criteria for BAC?

A. No, that's fine.

Q. Would you agree that's an acceptable definition of --

A. I think as we wrote it in here, and I just want to check. (Perusing.)

Q. I note you are flipping through the new WHO text. Maybe I can ask that this be marked as the next in order to see if this is the same thing and then maybe then we can make it part of the record?

A. All right. Sure.

(Defendants' Exhibit 22 was marked for identification.)

Q. BY MR. MURPHY: I'm going to hand you a copy of what's been marked as Exhibit 22 and ask you to see if that isn't a copy, at least in some form, of the WHO classifications for adenocarcinoma including the subtype BAC?

A. Yes.

Q. Page 36 of this excerpt --

A. Correct.

Q. -- it talks about bronchioloalveolar

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carcinoma?

A. Correct.

Q. It defines it as "an adenocarcinoma with a pure bronchioloalveolar growth pattern and no evidence of stromal, vascular or pleural invasion."

Do you see that?

A. Yes.

Q. Is that the WHO definition for BAC?

A. Yes.

Q. That is what you would use in diagnosing BAC?

A. Yes.

Q. It goes on and describes some other criteria in the paragraph that follows, and some of those criteria we just talked about in the Green article?

A. Yes, some.

Q. Are there criteria that are included in the WHO classification that weren't mentioned in the Green article?

A. Well, I think one thing that is present in the WHO classification is that there can be no invasion.

MR. RILEY: Just so the record is clear, you were looking at WHO and reading your actual text before then speaking. That was marked as exhibit --

THE WITNESS: It's 22.

MR. RILEY: Can we have for the record what page?

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THE WITNESS: The same page. It's very simple.

Q. BY MR. MURPHY: Aside from what you just pointed out about lack of an invasion in the WHO definition, are there any other differences between the two criterion?

A. No.

Q. Now, you answered a couple of questions already about BACs and whether they tend to appear in people that are younger or more likely to appear in females and whether people with BAC are less likely to be cigarette smokers.

Were your answers to those questions based on your own experience or your knowledge and review of the literature on BAC?

A. My own experience more than anything.

Q. Can you answer those based on your knowledge and/or review of the literature on BAC?

A. As far as -- I'm not sure I quite understand. As far as whether they tend to be younger and cigarette smokers?

Q. Yes.

A. I'd say there are examples of that reported, but I guess I haven't seen it myself. There are very few pure BACs as defined here. I think most adenocarcinomas of the lungs are patterns of different types of differentiation. They're very rare cancers in my own

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experience with the exception of the pure mucinous form and an occasional nonmucinous form. Most of them show variable features. All I would say is that I'm not sure I trust any of this until I had seen every case that they said they reviewed.

MR. RILEY: Just for the record, when you said "as defined here," you were referring to the original question?

THE WITNESS: Correct. Yes.

Q. BY MR. MURPHY: You understand, though, that in medicine and in pathology one would have to rely on studies that exist as part of scientific literature?

A. I agree with that, yes.

Q. You can't always review every piece of data that someone reviews on a study before you accept it as valid; is that right?

A. I agree.

Q. Have you ever attempted to do as Drs. Barkley and Green tried here and review the literature on BAC -- and not that it was their purposes -- but also review it with regard to whether it is associated with cigarette smoking or not?

A. I have only done it in the context of a practicing pathologist and perhaps more importantly as the chairman of the pathology section of the cancer study group.

Q. I wanted to at least continue through some of

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the article and ask whether you agree or not, and maybe we'll try to determine the sources of your disagreement if you have any.

On page 2379 of the article, do you see the left-hand column, the last full paragraph there, there's discussion about literature that showed an apparently inconsistent finding of an increased odds ratio for the development of BAC following quitting smoking. Do you see that?

A. I do see that, but that's also preceded by the sentence that they state, "Two recent case control studies have suggested an association between duration and intensity of cigarette smoking and the development of BAC." Then they make the statement, "Adding to the controversy, the case control study reported Falk, et al, showed an apparently inconsistent finding of an increased odds ratio of the development of BAC following quitting smoking."

To me that really strongly supports the hypothesis that cigarette smoke caused the disease because there are plenty of cases of lung cancer in people who have stopped smoking that are caused by cigarette smoke carcinogens. I think that is the precedents of "Cancer Prevention," Series 1; "Cancer Prevention," Series 2; every study that has ever looked at cigarette smoking and lung cancer.

Q. I understand your answer, but I want to try to limit my questions for a minute to: Do you agree that there

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is an increased odds ratio for development of BAC following quitting smoking?

A. I don't have any idea if that's true or not. All I can say is that, based on what this sentence says in this paper, that's true.

Q. You personally don't have idea of whether that's true or not?

A. I've never done an odds ratio on what incidence of BAC would be after people quit smoking. I guess the questions I would ask are: How long have they quit smoking? How many pack years have they smoked? What was the intensity?

Q. You read another sentence, and just for clarity we have a controversy term here that really goes back up to the paragraph beforehand. That started with, "The impact of cigarette smoking on induction of BAC is somewhat controversial."

Do you see that sentence?

A. I do.

Q. Do you agree with that?

A. I agree with that in general, yes.

Q. At the bottom of the paragraph we talked about a minute ago, the last full paragraph on page 2379, Drs. Barkley and Green state that, "More work to evaluate cigarette smoking as a possible etiologic agent in BAC needs

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to be performed."

Do you agree with that?

A. Yes.

Q. Does the next sentence note that "A viral etiology for BAC has also been postulated."

Do you see that?

A. I do see that.

Q. If I'm right, your book contains some reference to possible viral etiology for BAC, doesn't it?

A. It talks about Jaagsiekte.

Q. If you refer, I guess, to the first full paragraph on page 2379, the authors note that "BAC may arise in lung parenchyma damaged tuberculosis, pulmonary infection or abscesses, and pulmonary fibrosis of any cause," and they have in parentheses "rheumatologic, drug-induced, or idiopathic."

Do you see that?

A. I do see that.

Q. Do you agree with that?

A. Yes. But I would also say at the same time that very few of those cases really fall out as pure BACs. Most of them would be mixtures.

Q. Now, on page 2380, the authors discuss molecular biology. Do you see that?

A. I do.

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Q. Do you see they note and would you agree that "the role of oncogenes and tumor-suppressor genes in lung cancer is receiving much attention"?

A. Absolutely.

Q. They go on to say that "the prevalence of activated or overexpressed oncogenes or of mutated or deleted tumor-supressor genes in BAC per se has not been extensively reported."

Would you agree with that?

A. I would agree with that, yes.

Q. Do you know whether mutations of the P53 -- I believe it's a tumor-suppresser gene -- have been associated with BAC?

A. No. I don't know off the top of my head if people have even looked for that as far as a finding in BAC. I think what you can say in cancer, in general -- and I can refer you to two articles I happen to have with me -- is that if you look at the molecular biology of cancer that basically every solid tumor now is associated with at least two mutations of tumor-suppressor genes, one usually being P53.

So this idea that -- and I don't know that you were trying to say that, but I think it would be extremely, highly unlikely that you would not find a mutation of some type of tumor-suppressor gene in BAC because basically

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that's what causes cancer. It's the mutations in tumor-suppressor genes and proto-oncogenes that cause the tumors.

Q. Is it your opinion that cigarette smokers who develop lung cancer have a greater percentage of P53 mutations than non-smokers?

A. Who also have lung cancer?

Q. Yes.

A. I would say they probably do, but I would have to look that up. I don't know. There has been reports in Science and several other articles about possible specific mutations of P53 with respect to cigarette smoking, but I think we'd have to be very careful about that at this point in time.

Q. If you had a patient who had lung cancer and you could demonstrate a P53 mutation, one of the exons that's under study -- and I believe its 5 through 9 -- would you cite that as evidence supporting the determination that their lung cancer was caused by cigarette smoking?

A. At this point in time, I would have to look that up and see what the exact status of the latest research on that issue was.

Q. As you sit here today you just don't know?

A. I don't know for certain. That certainly has been applied, but from what I know and what I've seen myself

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in mutations of various oncogenes and tumor-suppressor genes -- I should say proto-oncogenes and tumor-suppressor genes -- there can be quite a bit of variability.

For example, you can see mutations in P53 in people that are exposed to asbestos who develop mesothelioma and don't have any history of cigarette smoking.

All I'm saying is that I would want to look that up. I really don't know what the answer to that question is. I'd have to study -- I'd have to evaluate that.

Q. If you had a patient with lung cancer and upon investigation it was determined that they did not have P53 mutations at Exons 5 through 9, would that be information that would lead you -- or be of assistance in concluding that their lung cancer was not caused by cigarette smoking?

A. I don't know. I'd have to look at that, also. I have seen cases myself of people who have developed lung cancer who have been cigarette smokers but not had those mutations. I don't know what that means, and I'd have to evaluate that or ask someone who is more knowledgeable than I am in molecular biology of mutations to answer that question. I would have to investigate it.

Q. If you recall offhand -- and we can try to find the exhibit if we need to -- I think it was Exhibit No. 2 which was the letter from Mr. Patrick to A.J. Singleton that talked about the fact that the plaintiff's

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had received the pathology that they eventually sent to you from the National Cancer Institute, do you recall that?

A. I don't recall that. Is this the letter you are speaking of?

Q. I believe it is, yes. If you see line 1, it notes "after receipt of pathology material from the National Cancer Institute."

Do you see that?

A. Yes.

Q. Did anyone tell you, or do you know from any source, why the National Cancer Institute had the pathology?

A. No, I don't know.

Q. Do you know whether anyone ever looked to see if P53 in Mr. Little was mutated at Exons 5 through 9?

A. I don't know.

Q. No one has ever told you whether that's been done or not?

A. No.

Q. You are not an expert on P53 mutations, are you?

A. No.

Q. You wouldn't hold yourself out to be one?

A. No.

Q. Let's turn back to the Green article on bronchioloalveolar carcinoma for a minute.

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A. Sure.

Q. Back to page 2379. Really, what we were talking about in some prior questions were the studies that showed an association between smoking and BAC and those that don't.

Would you agree with me that there are some immunological studies that show an association between smoking and BAC and some that do not?

A. I would agree with that.

Q. Can you turn with me to page 2383, which I think is the last textual page of the article?

A. Yes.

Q. In the final paragraph before the acknowledgment, about ten lines or so down, is a short sentence that reads, "The etiology of BAC is uncertain."

Do you see that?

A. Yes.

Q. Would you agree with that?

A. Well, I would maybe partially agree with that. I could probably say that etiology of all types of lung cancer in some instance, maybe with the exception of small cell lung cancer, is uncertain.

Again, I would say, the majority of cases that I have seen myself have been with cigarette smokers.

Q. The next sentence after that reads, "Prior

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pulmonary parenchymal damage, various occupational exposures, tobacco smoking, and retroviral infection have all been implicated."

Do you see that?

A. I do.

Q. And they have been implicated in the etiology of BAC, correct?

A. Yes.

Q. Would you agree with that?

A. Yes. I should qualify that. I have not seen any studies that retrovirus has caused BAC. I think if you look back to page 2379 he talks about viral etiology. He's first talking about the disease in sheep, and then the authors state on the top of 2379 in the right-hand column that "viruses have not been isolated from human BAC tumor cells, but intranuclear inclusions can be seen and, according to some investigators, resemble viral elements."

Well, they didn't do their homework. Those are surfactant inclusions and they're not viral inclusions. I mean, I can show you pictures in that book that show you exactly what they are. As far as I know there has never been any proof that viral inclusions have been seen in BAC. The reference they give in Reference No. 41 by Singh, "Carcinoma of Type II pneumocytes: Immunodiagnosis of a Subtype of 'Bronchioloalveolar Carcinomas,'" that he

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specifically talks about surfactant inclusions in the nuclei of those cells, and they're not viral inclusion.

I don't know of any evidence that there is a viral etiology of human BAC. I don't believe that in the sheep it was caused by a virus.

Q. If we take out the retroviral infection part of that sentence, would you agree with it then?

A. I would.

Q. Let me ask you to quickly turn to page 2379.

A. Okay.

Q. There is a section there entitled "Histopathology"?

A. Yes.

Q. And the first sentence is, "The histologic classification of NSCLC can be difficult."

Do you see that?

A. I do.

Q. And NSCLC is non-small cell lung cancer, right?

A. Right.

Q. Do you agree that the histological classification of non-small cell lung cancer can be difficult?

A. I believe there are instances where it can be difficult, yes.

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Q. Referring again to that sentence, as it continues on it notes that the subclassifications of adenocarcinoma of acinar, papillary, mucous secreting, and bronchioloalveolar are even more difficult. Do you agree with that?

A. In general I agree with that, but I think if people were to look at this book that's published it would be fairly straightforward. They'd understand two things: That the majority of the adenocarcinoma of lungs show various types of histologic differentiation and there are going to be several different patterns in any given adenocarcinoma, and there are going to be very few cases that are purely one pattern.

There are cases of both mucinous and nonmucinous BAC that exist as pure tumors, and there are a few cases of papillary adenocarcinomas that are pure adenocarcinomas. Most are a combination of all of these elements in reality.

Q. Authors here also note that increasing experience of the pathologist with BAC improves classification. Do you agree with that?

A. I agree with that, yes.

Q. Now, Doctor, you don't know of any entity, organization, publications, or anything else that theorizes that there are actually two different types of BAC, do you?

A. Could you ask that again, please?

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Q. Do you know of any entity, organization, or any publications that purports that there are two different types of BAC?

A. It depends. I can't answer that question like you've asked it. It depends on how you define types. Is that a histologic type or a microscopic type or what?

Q. It's a histologic type.

A. There's definitely two different histologic types. That's been reported in virtually every book that I know of.

Q. I'm sorry. There are different subtypes of BAC?

A. Yes.

Q. I guess what I'm getting at: Do you know of any entity or organization that says that there are two different BACs, two different entities called bronchioloalveolar carcinoma?

A. I, again, don't understand that question unless you can define entities for me. There are two microscopic patterns. There's one that occurs as a single nodule and multiple nodules, which is more common; and then there's another that occurs in a diffuse pneumonic form. I have some pictures of these in the book.

Is that what you mean by entities?

Q. Not really. We can go back to the chart,

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Exhibit 20.

Do you know of any classification scheme that, instead of listing BAC as a subtype of adenocarcinoma, would list it out on a level with the other four major cell types?

A. As a separate entity?

Q. As separate entity.

A. No, I don't.

Q. So you also don't know of any separate -- or any entity or organization that not only lists BAC as a separate entity under there but also as a separate entity and as a subtype of adenocarcinoma?

A. I don't know.

Q. Doctor, would you agree with me that tuberculosis can cause scarring in the lung?

A. Yes.

Q. Tuberculosis is an infectious disease?

A. Yes.

Q. It is not caused by smoking?

A. No.

Q. Histoplasmosis is an infectious fungal disease?

A. Yes.

Q. And histoplasmosis is not caused by smoking?

A. No.

Q. Histoplasmosis can cause scarring of the lung;

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is that right?

A. Yes.

Q. Pneumonia can also cause scarring of the lung, can't it?

A. Rarely.

Q. But it can cause scarring?

A. It can cause scarring, yes.

Q. Other occupational exposures like asbestos can cause lung scarring?

A. Yes.

Q. Now, there's a phenomena called scar cancers; is that right?

A. Yes.

Q. Scar cancer is a cancer that grows out of a scar in a lung; is that correct?

A. That's okay as a definition, yes.

Q. Scarring is associated with many cancers; is that fair to say?

A. Yes. The majority of scarring associated with most cancers is caused by the cancer and not preceding it.

Q. To be a true scar cancer the scar would have to precede the cancer?

A. That's correct.

Q. The cancer would have to grow out of a scar rather than the scar resulting from the cancer; is that

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correct?

A. That would be correct, yes.

Q. You would agree that, while there may be some lung cancers that produce scars, there are other lung cancers that clearly arise out of scars?

A. Extremely rare.

Q. You noted in your report -- do you still have access to it?

A. Yes.

Q. On the first page, in that second paragraph probably halfway down, the report notes that "there was a calcified spot at the top of the left lung which may have been caused by an old healed tuberculosis."

Do you see that?

A. I do.

Q. You have not reviewed the radiology that shows that old healed tuberculosis?

A. I have not, no.

Q. Or the radiology report?

A. First of all, I have not reviewed either one of those; but all I would say is that there is no way that a radiologist, by seeing calcification, can make a pathologic finding necessary for a clinical diagnosis.

There are many things besides tuberculosis that can cause scarring or can cause calcification. For example, one

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of the most common places that I see calcification in smokers is in the apical portion of their lungs in association with pleural fibrosis and subpleural elastosis and fibrosis.

For a radiologist to say this is previous tuberculosis is, I think, a guess.

Q. If Dr. Harley is the one who is making that determination would you say that's a guess too?

A. I would say that's a guess too, yes. I think that Dr. Harley stated that, "It may have been caused by old healed tuberculosis."

Q. Your report also notes two small nodules in the lower part of the right lung?

A. Correct.

Q. Do you have any opinion on what they are or were?

A. I don't, no. There's a variety of things that they could be, but I don't know what they are.

Q. If that calcified spot on top of Mr. Little's lung -- which Dr. Harley said could have been caused by an old healed tuberculosis -- existed before Mr. Little's cancer developed, then that was not caused by his cancer; is that right?

A. That would be true. Yes.

MR. MURPHY: Let's marked this in order.

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(Defendants' Exhibit 23 was marked for identification.)

Q. BY MR. MURPHY: Doctor, I'm going to hand you what's been marked as Exhibit 23 to your deposition. For purposes of the record this is an x-ray report dated 10/29/85, Bates No. 200409145-0010.

Have you seen this record before?

A. No.

Q. If you look at the first sentence of the description by the radiologist, he notes that "PA and lateral films of the chest reveal a calcified granuloma on the left."

Do you see that?

A. I see that sentence, yes.

Q. Do you know if that's the same granuloma that Dr. Harley talked about as being present in the radiology in 1995?

A. I wouldn't be surprised if it was, but I guess it always amazes me that radiologists think that they can make a pathologic diagnosis based on a shadow. A calcified granuloma implies some very specific things. It implies that there is definite granulomatous inflammation, which by definition is the accumulation of macrophasias, in this tissue with a calcium deposit.

There's a lot of things that can cause calcification without any granulomatous inflammation. I can't understand

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exactly how a radiologist can come to a pathologic diagnosis based on a shadow. That always amazes me.

Q. In fairness, though, you don't know Dr. Jones who made this --

A. I'm not saying anything negative against him. I see this all the time by radiologists. There have been many times that I would do lungs for people who have been diagnosed to have calcified granulomas, and they never have calcified granulomas. I'm saying that this is a pathologic diagnosis that radiologists make when they have no clue that this is a granulomatous inflammation.

Q. In any event, whatever this was and whatever is described in this exhibit was present in Mr. Little's lung long before his lung cancer; is that correct?

A. I agree with that.

Q. You can't sit here today and make a definitive determination one way or another whether what Dr. Jones saw in this film represented a calcified granuloma or not?

A. No, I can't. Nor can he.

Q. The letter from Mr. Patrick we marked that as 18; is that right?

A. Yes.

Q. He talked about some suspected metastasis?

A. He did, yes.

Q. What suspected metastasis did Mr. Patrick

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reference in his letter to you?

A. He stated that there were reports indicating that the tumor metastasized the liver and possibly the kidney indicating that the tumor grew outside of the lung. So I guess the liver and kidney were the two areas.

Q. You haven't seen any pathology for the liver or the kidney; is that right?

A. That is correct. It's my understanding, based on what he sent me, that that was based on this radiology report.

Q. You've seen the radiology report. What does that describe regarding the kidney or liver?

A. It says with respect to the liver that limited views of the upper abdomen demonstrate visible increase in hepatic -- hepatic and the liver are the same -- hypodensities compatible with progressive metastatic disease. Then he states in the posterior segment of the right lobe -- I think No. 40 -- there is a lesion measuring 3.2 by 3.3 centimeters, previously measured 2.7 by 2.9 centimeters.

Then the final sentence in that paragraph reads that there are several small left renal hypodense lesions, but once again they are too small to accurately characterize by CT.

Q. So the radiology report refers to

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hypodensities in the liver and in the kidney?

A. Right.

Q. The radiologist can't make a diagnosis of a cancer in those organs based on radiology, can he?

A. No. But they can diagnose granulomas in the lung.

Q. That's what I was going to get to.

A. No, they can't. I didn't mean to be wise. I'm sorry.

Q. It's the same point, though?

A. It is the same point. You're right.

Q. Hypodensity is not the equal of metastasis?

A. Not necessarily. The thing that you need to be concerned about would be the liver where the change over time is showing an increase in size. That wouldn't happen in most other pathologic conditions, but it could. It could happen like in an abscess or something like that. It would be possible.

Q. As a pathologist, though, you would want to look at pathology for the liver or the kidney before stating your opinion on whether there was cancer present in those organs, wouldn't you?

A. If you wanted to be certain, the answer would be yes. Everything has to be taken in a clinical setting whether or not that's indicated, which in most instances it

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would not be. Yes, you want to know that just like you would want to see that lesion on the upper lobe of the left lung to see if it truly was a granuloma.

Q. None of those may have been indicated in the clinical setting; is that right?

A. That's correct. It kind of depends on what the person's condition is; and if I understand the reading of the records I have and Mr. Patrick's letter, this man basically died from metastatic lung cancer. That's what it sounds like.

Q. And we're talking about at this time. We are in the litigation setting now, right?

A. I understand that.

Q. And there are ways that we could have gotten pathological material from the kidney, from the liver, and from that suspected granuloma in the lung, aren't there?

A. Well, the granuloma in the lung should have been evaluated when the left upper lobe was dissected, and I don't know exactly why it wasn't.

With respect to the kidney and liver, technically and theoretically, yes; but practically, no. I don't know of any insurance companies that would pay for that type of thing to be done. If this man died and he had an autopsy, the answer is obviously yes.

Q. You know that this man did die, right?

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A. Is he dead?

Q. It was in your report or some of the records.

A. I guess I forgot about that. I knew that. Sure, I knew that. I forgot.

Q. You forgot about it, but you know that he's dead, right?

A. Right.

Q. Do you know whether he had an autopsy or not?

A. He did not.

Q. Certainly an autopsy could have been performed on Mr. Little?

A. It could have been, yes.

Q. If it was performed we would have further evidence about this possible metastasis in the kidney and in the liver and about this possible granuloma in the left upper lobe, correct?

A. The autopsy for the granuloma is not going to help because the left upper lobe had been removed and been destroyed. But the other things the answer is, yes, you could have found out about them.

Q. If you did an autopsy you may have been able to collect more tissue from the lung for determination of what cell type the lung cancer was; is that right?

A. Yes.

Q. There is no doubt that an autopsy would have

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provided more information about Mr. Little's cancer?

A. I would agree with that.

Q. Now, we talked about the Butler case at the beginning of the deposition; do you remember that?

A. Right.

Q. That was the smoking case you got involved in with the Ness, Motley firm?

A. Initially, yes.

Q. In the Butler case you actually went to Mississippi and did the autopsy on Mr. Butler after his death; is that right?

A. Yes.

Q. Similar to this case, litigation had been filed before Mr. Butler died, and you went and did the autopsy as part of your role in that litigation; is that correct?

A. That is correct, yes.

Q. Now, if someone from the Ness, Motley firm had asked you to go to South Carolina and do an autopsy on Mr. Little's body, would you have done so?

A. Probably, yes.

Q. Now, another case that we mentioned at the beginning of the deposition was the Gilboy case?

A. Yes.

Q. An autopsy was done in the Gilboy case; but

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just for clarity, you didn't do it?

A. That is correct, yes.

Q. But you know that, similar to the Butler case and this case, during the course of litigation Mr. Gilboy died and an autopsy was done after his death; is that right?

A. That's correct, yes.

Q. And you know that in the Gilboy case it was alleged that Mr. Gilboy had lung cancer during his lifetime. Putting to the side the question of whether he had it or not, you know that during the autopsy it was determined that there was no lung cancer present in his body at that point in time?

A. That may well be true, but that's not uncommon especially in a person who has had his type of clinical history. Mr. Gilboy actually had metastasis to his brain about seven years before he died, which is something that would occur in probably less than a tenth of a percent of people with lung cancer. He was treated for his primary tumor and he was treated for metastatic tumor, so it's not necessarily unthinkable that he wouldn't have any evidence of a primary tumor in his lung when he was autopsied.

Q. There was some surprise, among the clinicians at least, that Mr. Gilboy's autopsy revealed that there was no cancer in his body?

A. I don't know whether there was or not. That

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wouldn't surprise me because of the fact he had lived seven years after he had a brain metastasis and the fact that, as far as I could tell from the information that was supplied to me, that he had no evidence of tumor elsewhere in his body at the time of his death.

Q. Leaving the Gilboy case to the side, autopsies can and do sometimes provide what is known as an autopsy surprise; is that right?

A. Yes. Yes, they can provide surprises. I think the Gilboy and the Butler cases were different than this case. The Butler case was an alleged case of environmental tobacco smoke causation of lung cancer. This is totally different than this case, and it was totally different in the Gilboy case as far as the smoking history or the smoking situation.

In the Gilboy case it was a very interesting case because of the fact he had survived so long after the primary tumor was treated and after the brain metastasis was treated.

Q. In Gilboy, though, you did look at the results of the autopsy in forming your opinions on the cause of Mr. Gilboy's lung cancer?

A. I don't think it was so much the autopsy as far as the cause. I think the cause really had to do with the smoke he consumed and it's really about the smoking

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situation. To be quite honest, I can't remember all of the details on the Gilboy case autopsy without going back and looking at that file.

Q. I just want to go back and talk a little bit more about what we called autopsy surprise.

A. Okay.

Q. You can, on autopsy, find a cancer you never knew the patient had during his lifetime?

A. It's possible.

Q. And there's literature that documents the frequency of that happening, isn't there?

A. There is.

Q. You can also find on autopsy, on occasion, undiagnosed primary tumors that you didn't know about during a patient's lifetime?

A. It's possible, yes.

Q. Let me just back up for a minute on something you mentioned about the granuloma in the left upper lobe. I think you stated somewhere along the way that, if we wanted to evaluate that granuloma, the surgeon should have taken a pathology sample of it at the time of the surgery on the left upper lobe?

A. No. I think I said -- let me be sure.

(Perusing.)

If I understand the pathology report right, the left

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upper lobe was dissected on March 11, 1996.

Q. And the granuloma was present at that point in time?

A. I mean, if it was present in 1985 and referred to by other people as being present, I would think that it would have been present. The only thing that I saw in his pathology report was basically the description of the tumor and how close it was to various structures, which is very important because I had to do staining.

Then it talked a little bit about the uninvolved lung parenchyma, but I didn't see any description given in that report unless I'm missing something which is always possible.

There was a distinct calcified nodular at the apex of the left upper lobe. They stated in the pathology report that there was a ten by four centimeter of roughened pleura at the apex, and I would think that was probably due to adhesions -- probably due to emphysema. there was a nine by five centimeter area of cloudy gray pleura in the lower portion of the left upper lobe.

I didn't see any description given of a separate granuloma -- a supposed granuloma. If you don't see something, you can say two things: you don't know if somebody didn't look for it and they didn't find it or if they didn't really look.

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A lot of times what happens when a lung is receptive to lung cancer is that the only thing that people pay attention to is the lung tumor, and that's rightly so to a certain degree because that's the most important thing because it can really affect how the patient is treated. I don't really have any argument with what they did.

Q. Let me try to sum this up. From the records you have, you don't know whether the surgeon who did the lobotomy -- is that the right word?

A. Lobectomy.

Q. -- lobectomy on the left upper lobe looked for the granuloma or not at that point in time?

A. I don't think it should have been the surgeon. The surgeon is just acting as a technician to get rid of the tumor. The surgeon doesn't care, really. I shouldn't say that quite that way. They are basically trying to remove the tumor in a way that is a sufficient cancer operation. He may not have even known if there was this nodule in the left upper lobe that was stated to be a granuloma.

It's not a surgeon's responsibility to biopsy that or do anything. It's the pathologist's responsibility when they get that specimen out to adequately examine the entire specimen. What I'm saying is that often what happens is that the pathologist frequently will just hone in on the tumor which is the most important part of the specimen and

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sometimes not look at the rest of the tissue.

MR. MURPHY: They've brought coffee, so let's go off the record for a couple minutes.

(Recess taken.)

Q. BY MR. MURPHY: Doctor, I want to again refer you back to something you said at the beginning of the deposition about a case in litigation where you may not have concluded that a smoker's lung cancer was caused by his or her prior cigarette smoking. I think you mentioned an instance where the time between when the person had quit smoking and when they had developed their lung cancer was sufficient enough that you did not think the smoking -- or at least you couldn't conclude that the smoking was causally related to the lung cancer. Do you recall that?

A. Yes.

Q. And you are familiar with the concept of declining risk?

A. Yes.

Q. In general, the longer one has quit smoking the lower their risk of lung cancer caused by their cigarette smoking becomes?

A. In general, yes.

Q. And you agree with what the Surgeon General said in 1981 that after ten or so years of quitting smoking the risk of lung cancer begins to approach that of a

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nonsmoker; is that right?

A. I'm not familiar with that. I thought that the chart that I put in my book was the one that was taken from the 1989 Surgeon General's report that shows that after approximately 20 years the risk goes down to about two times that of a nonsmoker.

It's shown on Figure 1-2 which may be 32-2 in yours. It's right towards the very beginning of the chapter that talks about etiology.

Q. Maybe that didn't make it.

A. Keep going a little bit more. That one in the upper --

Q. Okay. That's lung cancer mortality ratio, correct?

A. Right. That's not exactly the same as risk but...

Q. You are referring, for purpose of the record, to page 1128 of the Dail and Hammar text, Pulmonary Pathology, second edition?

A. Yes.

Q. That's a reprint of a graph from the 1989 Surgeon General's report?

A. Correct.

Q. Now, given that the concept of declining risk -- let me back up for a minute.

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From Mr. Patrick's letter to you, Mr. Patrick indicated that in the 1970s Mr. Little had switched brands of cigarette from one to another; do you recall that?

A. I do.

Q. Given the concept of declining risk if, instead of switching brands in the '70s, as Mr. Patrick noted, Mr. Little had quit smoking, is it your opinion that he would have developed lung cancer in 1995?

A. You never know. I don't think there's any way to say one way or the other, and I don't know of any way to sort that out statistically. He may have; he may have not.

Q. Can you say to a reasonable degree of medical certainty if Mr. Little had quit smoking in the 1970s instead of switching that he would have developed lung cancer?

A. No, I don't think I could say that.

Q. How old was Mr. Little at the time the lung cancer was diagnosed?

A. Fifty.

Q. Do you know how long the tumor was present in Mr. Little's lung?

A. Not exactly. All you can do is make some assumptions and -- let me start that over.

I can't say exactly. The only way you can look at that is from what has been published concerning the average

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doubling time of this type of tumor, and assuming that the linear growth is based on that you can maybe get some type of an idea based on what the pathology report stated the size of the tumor was.

Q. Have you done that?

A. No.

Q. As we sit here today, can you in any way estimate when the tumor may have occurred?

A. I can probably estimate. I think the tumor has a maximum dimension of 4.2 centimeters. (Perusing.) Assuming that maybe was average, and say a 3 centimeters spherical mass and if you assume that cancer cells start out at 10 micrometers in diameter and that it's expansion is one cell divides into two, two cells divides into four, et cetera, that takes ten doublings to produce a tumor that's 1 millimeter in diameter and has a million cells in it and it takes 20 doublings to produce a tumor that's 1 centimeter in diameter that has a billion cells and it take 30 doublings to produce a tumor that is about 3 centimeters in diameter that has, I believe, over a trillion cells.

Then, if you assume -- I guess the question is how you would classify this tumor. We'll just say we will classify it as a large cell undifferentiated carcinoma, and I will quickly look up in my book to see what I wrote in my book to see what I wrote in there with respect to what the average

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doubling time or the range of doubling time was or is for that type of tumor.

Q. Can you give me the section?

A. It would be on doubling times of lung neoplasms. It would be after histologic classification.

Q. Okay. I have it.

A. The comparison of data on doubling times of primary lung cancers.

Q. In the Pulmonary Pathology textbook it's Table 32-16.

A. There are two different times given. Look at Table 115. The average doubling time of undifferentiated would be 86 days. That's large cell. Right next to it is small cell lung cancer. That's 86 days. If you look at this other table from another paper, the average doubling time for large cell is 111 days.

Let's average those two. That's all about a 100-day doubling time. By the time it was diagnosed there had been 30 doublings, so multiply 100 by 30. That would be 3,000 days. Then if you divide 3,000 by 365, that would give you how many years. That's about eight years -- a little bit over eight years.

Theoretically, if you make those assumptions that the tumor grew in a linear manner, the doubling time was always the same, and that the doubling time was 100 days. His

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tumor, if you assumed that it was 3 centimeters in diameter when it was removed, it would have been in existence for 8 years prior to when he -- that would be eight years minus 1995 or 1996.

Q. So back in 1987 or '88?

A. Yes, 1987 or '88.

Q. Can you state to a reasonable degree of medical certainty that the lung cancer in Mr. Little's lung was not in existence at the time when he switched brands of cigarettes in the 1970s as referenced by Mr. Patrick?

A. If you assume this to be true, you could say that the lung cancer was not in existence, but what you couldn't say would be that the mutations that were occurring, proto-oncogenes and the tumor-suppressor genes that eventually led to the lung cancer, were not in existence.

I believe that they were in existence and that the process started very close to the time when he first started cigarette smoking, but I can't tell you the sequence and I don't think anybody can of how long it takes for a mutation for proto-oncogene or a tumor-suppressor gene to occur.

Q. It's your opinion, though, isn't it, that cancer starts with the mutation of a single cell?

A. No. I don't think it's a mutation of a single cell. It depends on how you define cancer. If you say that

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the cancer begins when the first cancer cell was created, that's what we'd be talking here; the first cancer cell was created, theoretically, in '87 or '88. If you look at the process by which it took to cause to this cancer cell, it was in existence basically from the first time he started smoking.

Q. But the mutations that we're talking about -- I probably used the word incorrectly -- those are those oncogenes and tumor-suppressor mutations?

A. The proto-oncogenes and the tumor-suppressor genes, yes.

Q. Those mutations are not cancer, are they?

A. Well, it depends on how you look at that. I would just refer you to these two articles. I refer to "The Hallmarks of Cancer," and that's published by Douglas Hannahan (phonetic) and Robert Wienberg (phonetic) in a cell, Volume 100, pages 57 to 70, January 7, 2000. If you look at what they say, basically this process starts to develop and develops over a long period of time, and it takes numerous mutations of various genes and eventually we see the development of a single cell that then expands.

I look at it that in a person who smokes -- just like asbestos, if a person develops a cancer, the cancer started when they first were exposed to cigarette smoke or asbestos in the case of mesothelioma.

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Q. There is no way, as you sit here today, you could go back and tell me when the first mutation to a tumor-suppressor gene or oncogene occurred in Mr. Little's case, is there?

A. No, I could not.

Q. Now, based on the calculations you just made and I think some of your other testimony, do you know when Mr. Little's cancer would have first been first visible on a chest x-ray?

A. I would say, potentially, it would have been first visible after about 20 doublings which would be 1 centimeter.

The CT scan now has resolution down to about 5 millimeters, but that's not always going to pick up. I think that people that have gone back to standard x-rays and have known that a person has a tumor, they would look back and tried to determine when it was first present retrospectively.

About the first time you will see it is about a centimeter. That was after 20 doublings, so that would be 2,000 days divided by 365. That would be about five-plus years, so that would be 1991 or 1990.

MR. MURPHY: Let's mark this as the next in order.

A. Let me also say that's the ideal. It turns out people that have lung cancer most of them are diagnosed

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at about 3 centimeters.

(Defendants' Exhibit 24 was marked for identification.)

Q. BY MR. MURPHY: Doctor, could you tell me what size Mr. Little's tumor would have been about 1993?

A. In a perfect world, based on these calculations, it would probably have been maybe in the neighborhood of about 2 centimeters.

Q. Let me hand you what we have marked as Exhibit 24. For the record I'll state that this is a radiology report dated June 2, 1993, Bates No. 200409098-0003.

Have you seen this record before, Doctor?

A. No.

Q. I want to direct your attention to the sentence that starts the fourth line from the bottom of the description there. The sentence reads: "There is a 1.5 centimeter nodular density overlaying the left second anterior rib, which likely represents an intraosseous process, but a pulmonary parenchymal nodule cannot be excluded."

Do you see that?

A. I do.

Q. Do you see that the x-ray taken on Mr. Little in June of 1993 revealed this 1.5 centimeter nodule or density that the radiologist thought could be a tumor, correct?

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A. Yes.

Q. While it's not an exact science, that 1.5 centimeter measurement is pretty close to what you calculated the size of Mr. Little's tumor would have been at that point in time?

A. That is correct.

Q. I know you haven't seen this before but just having seen it, would it be your opinion that what the radiologist saw in this x-ray was what was eventually diagnosed as cancer in Mr. Little?

A. I would say it's a good possibility, but the other thing that one would want to do would be to go back to the more recent x-rays and see if the location of the mass, as it was defined, was the same prior to when he had the initial diagnosis and treatment -- see if it was in that same location. That's what you would want to determine, but my guess would be there's a good chance that that was the tumor.

Q. Now, the radiologist recommended another view film?

A. He did.

Q. You don't know if more films were taken at this time, do you?

A. No.

Q. The radiologist also noted possible pneumonia.

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Do you see that?

A. I do see that. I don't quite -- I do see that, sure. I don't know exactly -- I'm not a radiologist. I don't know exactly what that means other than just what it says.

Q. And the radiologist again noted that a follow-up radiograph would be of benefit with regard to that pneumonia?

A. Yes.

Q. You don't know if there was ever any follow-up at that time, do you?

A. I don't know.

Q. Again, this -- not to pick on the radiologist, but this radiologist also noted a single granuloma in the left lung. Do you see that?

A. I know that.

Q. They are at least consistent, aren't they?

A. They are consistent, yes.

Q. In June of '93, when this x-ray report was taken, Mr. Little was approximately 48 years old?

A. Yes.

Q. Whether the tumor was first visible when Mr. Little was 48 or thereabouts, his cancer was diagnosed at an early age?

A. Yes.

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Q. I think that somewhere in your file there's a cover letter that claims to be submitting to you the description or reports from the defendants' experts. I think you testified that you don't recall receiving those?

A. I don't think --

Q. I don't want you to go through them.

A. Did you see --

Q. I did see a cover letter, but I didn't see any listing of the experts.

A. Maybe it's something I don't remember.

Q. Do you know a Dr. Peter McCue?

A. No.

Q. Do you know a Dr. Barsky?

A. I know his name. I don't know him personally.

Q. Do you know him by reputation?

A. I little bit, yes..

Q. I believe you cited a few articles in your textbook by Dr. Barsky?

A. I did. Yes, I did.

Q. Have you come across his name in scientific literature?

A. I have.

Q. Does Dr. Barsky have a good reputation?

A. As far as I know, yes.

Q. Do you find him to be accurate in his

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published writings?

A. You know, I can't think off the top of my head exactly what he's published. I'd have to go back and look. I think there are some articles that were cited in that one review paper you gave me, which was the one by Drs. Barkley and Green. Yes, Reference No. 7.

Q. In your own text you probably don't remember specific references to Dr. Barsky; but, in general, you wouldn't cite studies that were not reliable, would you?

A. I would try not to. Most of the articles that I've cited in my book are peer review articles, and you would think they were legitimate and reasonable articles.

Q. Do you know Dr. Green, one of the authors of that article on bronchioloalveolar carcinoma?

A. I do not.

Q. Do you know that Dr. Green was one of Mr. Little's treaters?

A. I do not know that, no.

Q. Now, at one point in time, you pulled out two articles from your briefcase, and I think you read one into the record. Would you read the second one in. The title and --

A. I didn't read the second in. Do you want me to?

Q. Please.

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A. It's called "Cancer of the Emerging Molecular Biology" by Dennis W. Ross, University of North Carolina.

Q. Read in some bibliographic information so we might find it.

A. It was published in Hospital Practice, January 15, 2000. Let's see if I can find --

Q. That's probably sufficient.

A. I don't see a volume number. This is kind of more of a lay-type of journal. I don't know -- I'm sure it probably has a volume, but I don't see it.

Q. One question: As we were going through the day you've been making some handwritten notes on a pad. What are those?

A. Those are the things I'm going to do just from some of the questions that you asked me.

Q. Would it be possible for us to make that an exhibit? Like the other materials we'll get the original back to you, but we'd like a copy of it for the records. Do you have any objection to that?

A. I don't think it's anything that you really need. It's just a list of things that I was going to do myself.

Can we read them in maybe?

MR. EVANS: Why don't we so that Dr. Hammar can hang to it.

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MR. MURPHY: Sure.

A. The first one is labeled cigarette smoke and lung cancer threshold. By that I wanted to just review the literature about whether there is any threshold involvement. Lung cancer does not show an increased risk in people that are smokers.

Number two was the large cell undifferentiated carcinoma of the lung and cigarette smoking, and I have a note to check CPS, CP1 and CP2.

Number three is BAC and smoking, and I have a note to myself to review all literature, do a MEDLINE search on smoking and BAC.

Number four is the Garfinkel and Auerbach study. I have a note to review it with respect to smoking and BAC.

Number five has to do with P53 mutations and smoking. I have a note here to check on that.

That's it.

Q. BY MR. MURPHY: Can I refer to that as sort of a task list that you made based on this deposition?

A. It is, yes. It's certain things that I'm going to do just mainly because I'm interested in it and because, if I'm asked questions about that at trial if I'm involved, I would kind of want to review that.

Q. Are you planning to do those task on that list before testifying at trial?

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A. It kind of depends on what Mr. Evans and Mr. Patrick want me to do. A lot of these things that I'm interested in are in subjects that they have people that are far more expert in than myself to discuss. It wouldn't necessarily be what I'd talk about at trial. They have epidemiologists, for example. They have people that know a lot more about this than I do. I think what I know a lot about is pathology.

Q. If you do do those tasks and come to any conclusions on those, would you let Mr. Evans know so that he can tell us? Do you have a problem doing that?

(Request for production.)

A. No, I don't.

Q. BY MR. MURPHY: I'm going to turn the questioning over to Mr. Riley. Whether I tell you now or tell you later, I'm going to say that we're leaving the deposition open because the court is going to be ruling on some matters that may affect the extent of testimony or may affect what some of our experts do based upon Dr. Hammar's work.

I'll pass it forward.

MR. RILEY: Let's go off the record for a second.

(Pause in the proceeding.)

MR. RILEY: The understanding was that Dr. Hammar brought with him some projection slides, pictures that he

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took of the tumor. We do not have actual photographs that we can look at today, and we seek the opportunity to ask Dr. Hammar about the slides that he took when we have prints.

MR. EVANS: I'll just say on the record that I realize that there are matters before the court that may affect this witness. As far as the slides, I think Dr. Hammar made it clear that he was prepared to identify today what was on the slides. While he did say that obviously there's more detail on a printout, I don't think -- it would be our position that that wouldn't justify addition deposition time.

MR. MURPHY: I don't want to cut you off. I think enough has been said on the record about that, and we refer to the record. I just want to let you know that we don't agree with your position.

With that we can move on.

EXAMINATION

BY MR. RILEY:

Q. Doctor, if it's okay with you, I'll stay at this end of the table.

A. That's fine.

Q. Doctor, one thing you said that you might do on your task list was to look at whether there is a threshold for exposure to cigarette smoke in order to result

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in cancer?

A. Yes.

Q. What sources would you look at in order to make that determination?

A. Well, I guess I'd probably go back to some of the initial articles I have which I've cited in this book under the etiology section of lung cancer to see if there are examples there of looking at people who have like, say, low pack years of cigarette smoking with respect to how frequently they get cancer versus the nonsmoker. I'd probably just do a MEDLINE search and basically ask for articles dealing with the incidence of lung cancer in people with a low pack year history of cigarette smoking or something like that.

Q. As you sit here today are you able to testify whether smoking cigarettes for a period of six months, let's say, the amount that Mr. Little smoked, creates a substantial increased risk of lung cancer?

A. The best knowledge I have without looking anything up would be that it does not.

Q. That's your current opinion?

A. That's what my opinion is based on what I've observed myself and what I have written.

Q. Do you have any basis, Doctor, for opining in this case that Mr. Little's smoking of Barclay cigarettes

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was a substantial contributing cause of the lung cancer in 1995?

MR. EVANS: I will object. I think the question is probably outside his area of expertise.

MR. RILEY: Okay. Well, I'll withdraw the question. Are you telling me you don't intend to elicit testimony from Dr. Hammar about whether or not smoking Barclay cigarettes was a substantial contributing factor? If you're not, I'll withdraw the question.

MR. EVANS: Well, I'm going to rely on the report of disclosure that's already filed in this case. I just wanted to state that objection for the record, and Dr. Hammar can answer.

A. All I'd say is that all carcinogens contribute to the development of cancer. When you're talking about a multi-stage process of carcinogenesis, it's that any exposure to that carcinogen I think potentially contributes. Now, how much it contributes is very difficult to say.

Obviously, if you compare six months of Barclay versus the other cigarette smoking he had, it's a very minimal exposure; but you never know, though, that maybe that was the key one that did the final mutations that made a cell change.

Q. BY MR. RILEY: Can you offer testimony to a reasonable degree of medical certainty that it is more

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likely than not that smoking Barclay cigarettes contributed to any of the mutations that caused Mr. Little's cancer?

A. I cannot do that myself. No, I cannot.

Q. If instead of smoking Barclay cigarettes for that six-month time interval, if he had stopped smoking altogether, can you say whether or not his disease process would have been different to any material extent?

A. I could not say.

Q. Now, Doctor, how long did you spend reviewing your pathology slides and pathology materials in this case before you issued your report?

A. I spent a total of two and a half hours reviewing this case. What I usually do is, first I review all of the medical records that I have -- the written material -- and that includes the things like whatever reports I have. Sometimes I wouldn't necessarily refer to them, but I would have reviewed those.

Then I review the pathology materials to see what I see, and I always correlate that with reports as best I can. Then, if I thought there were any specialized tests to do, I would do that, which I did in this case. Then I would usually dictate the report.

Q. You say you spent two and a half hours reviewing the medical records.

A. A total.

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Q. How does that compare to a physical patient that you see?

A. Well, it's an entirely different situation. With an individual person what I do basically is an acquisition form saying this is the type of specimen that you have and what we are asked to do is to provide a report. The clinical history, if it's not available, I usually call up the doctor. In fact, I did that last week, for example, where they didn't give me a clinical history on this man who had an empyema, and I wanted to know if he had had a centrally located lung cancer that was causing the empyema. I called up the clinician and asked him about that. He didn't know, so then I had to find out from the pulmonologist.

Every case is different, but normally to do a lung cancer case, if I just did the gross and the microscopic, in most instances, with my degree of experience at this point in time, it would probably take 45 minutes.

Q. Now, when you did your review in this case did you make voice recordings?

A. No. I dictate -- once I have reviewed the records and the pathology then I would go back and dictate the report. I didn't make any kind of preliminary dictations other than -- there's always going to be some typos and there's always going to be things I missed -- and

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some you have already pointed out. I try not to let that happen, but it happens. It will happen in maybe one or maybe even two drafts that I'll just toss when they are done. But they're not significantly different from the final.

Q. Just to correct typos and that type of thing?

A. Right, exactly.

Q. You don't make notes to try to refresh your recollection for when you go to dictate your final report?

A. No. I try to do it all at one time so I really am concentrating on that case. Sometimes I will dictate up to a point where -- say, we talked about the immunohistochemistry. That might take a few days to do and then I'll start again separate, but everything else that I've dictated until that time has been transcribed.

Q. Did you make any written notes regarding your review of the records or pathology?

A. No.

Q. Who actually took the pictures that you brought with you here today?

A. I did.

Q. And you decided what areas of the tumors to photograph?

A. Yes. The tumor is pretty much all the same in the SP96-4435 and pretty much the same in the 96-16688.

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There wasn't too much variation. I just took the blocks from the resection that I had the most of and took photographs of that, but it was pretty much the same.

Q. What was the basis for the areas that you selected for your photographs?

A. Basically, the basis was that there wasn't a whole lot of viable tumor left in the resected tumor in 1995, so I found the slides that had the most viable tumor in it and they were the ones that I took the photographs of. It was pretty much the same. It was a relatively small four-sided tumor surrounded by this very intense fibroinflammatory reaction.

Q. You said that you believed the tumor showed keratinization in the intercellular junction?

A. I did.

Q. Were those features readily apparent to you?

A. In some of the areas, yes.

Q. But not in all of the areas?

A. Not in all of the areas, no.

Q. Is it possible, Doctor, for adenocarcinoma to show distinct features?

A. Intercellular junctions can be seen in between most epidural cells. It just turns out that in squamous carcinoma you have far more intercellular junctions and they're easier to see. You can see what actually represents

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the intercellular junctions but they don't appear the same, and that's just because the actual squamous cells have their growth processes that are the prickles that sometimes they digitate or they're more easily defined in squamous carcinoma.

With respect to keratinization, keratin is present in virtually every epidural cell there is, but the degree of keratinization and what you see in squamous cell carcinoma is much more pronounced.

Q. If I understand your testimony, then, it's not the presence of the keratin or the junction, it's the degree?

A. It's the degree and the way they are arranged, yes.

Q. What is it about the way they are arranged?

A. With squamous cells, they are usually arranged all the way around the cell. If you look at it in three dimensions, it's hard to cut the cell and use it. There would be connections between all of these. If you look at a tennis ball that had little spikes sticking out, there would be an adjacent tennis ball that had spikes coming down. That's one of the things that squamous cells do.

Q. But adenocarcinomas show these same features at least to some extent.

A. You don't see the junctions in adenocarcinoma.

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I guess part would be due to the fact that you're looking for gland formation which is the feature of an adenocarcinoma.

Q. You're just looking for something different?

A. Looking for something different or the way the cells are arranged like in a classic BAC or mucinous or nonmucinous. Cells are growing along the alveolar septa or riding next to one another and the junctions would be primarily right at the very tip. That's called a junctional complex. You don't see it like you do when you have all of these interdigitating processes like in a squamous carcinoma.

Q. When you provide your photographs -- you said you'd have copies made and give them to each of us and you also said that you would label them and number them the same way they are in your set --

A. Yes.

Q. -- would you also for us identify which of the slides it is that show the keratinization and the prickles?

(Request for production.)

A. I will, yes.

Q. BY MR. RILEY: Doctor, you told us that the immunostains that you performed showed that the tumor was negative for surfactant apoprotein A-1 and TTF-1, right?

A. Yes.

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Q. Is the fact that neither one of those stains were negative rule out the possibility that this tumor arose from a Clara cell?

A. No. Not 100 percent certain, no.

Q. To any reasonable extent can you rule out the possibility the Clara cell was sole genesis for this tumor?

A. I would say that the majority of tumors that I have diagnosed as BAC that I've done a Factor 1 on, which is a commercially available antibody, that those tumors are positive.

Now, have I gone back and made sure that every one of those is a Clara cell? No. By ordinary light microscopy, it would very hard to tell, say, Clara cell from a Type II pneumocyte. They can look very similar. The ones that I think look like Clara cells -- Clara cells have been TTF-1 positive.

Q. The majority?

A. The majority, yes.

Q. But not all?

A. Not all of them.

Q. Can Clara cells give rise to BAC, doctor?

A. Yes.

Q. So the fact that this tumor was negative for surfactant apoprotein A-1 TTF-1 does not definitively rule out BAC carcinoma arising from a Clara cell; is that

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correct?

A. I don't know for -- I would say that that is probably correct. What I don't -- and that's another thing I'm going to put on my list to review -- is that Clara cells produce a variety of different secretory products, one of which is a surfactant-like product. I don't know if the surfactant-like product that is produced by Clara cells would cross react with the surfactant apoprotein A-1 antibody. I don't know. I would have to look that up.

Q. Where are you going to look that up?

A. I'll start again with that review article by Singh, and then I'll call up my friend Allen Gown and see if he knows, and then I might even get into some more detailed literature in that review article by Singh where they talk about secretory products of Clara cells. I think I could find that answer.

Q. If you do do that research and you talk to Dr. Gown, would you please let the Ness, Motley firm know so that they can let us know?

A. I will, yes.

(Request for production.)

Q. BY MR. RILEY: Which of the two stains, Doctor, is more important to you or more significant to you in terms of your assessment of the type of cancer it is in this case? Is it the TTF or the surfactant apoprotein?

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A. Actually, it's neither. It's the histologic appearance of the tumor.

Q. Why is that?

A. Well it looks like a squamous carcinoma, the majority of them.

Q. In other words, the stains don't count the histologic appearance?

A. Well, you know, these to me would be what you expect of this type of tumor. They would be negative in squamous carcinoma because squamous cell carcinomas don't produce thyroid transcription factor I, or surfactant apoprotein A-1. If you were just to go on the immunohistochemistry and not anything else, I would say that it's TTF-1.

Q. Doctor, you would agree with the statement that the World Health Organization uses light microscopic criterion for classification of tumors?

A. Yes.

Q. Does the WHO-2 or the WHO-3 recognize that immunostaining can be used to determine whether or not a tumor is BAC?

A. (Perusing.) Maybe I'll just read what it says in here. I think that's the best way to answer the question. On the first page of the introduction, in the bottom paragraph where it starts out with the definitions of

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the tumor types. Then it goes over to page 4 which it states on the last sentence in that continuing paragraph, "However common criterion and the present classification are designed to categorize most tumors largely by conventional methods."

It's my understanding from being involved in this and doing this that this book, again, is based primarily on light microscopic histologic appearance; but this book, again, was more like the previous ones, just purely histologic appearance.

Q. Would you agree with this statement that light microscopy morphology is the manner in which lung cancers are classified histologically?

A. I'd agree with that. Histologically means looking at something through the light microscope.

Q. Would you agree that the classifications of lung cancer according to light microscopy were used by epidemiologists in determining causal relationships?

A. I would agree with that, too.

Q. You talked to Mr. Murphy a little bit this morning about interobserver variability; is that correct?

A. Yes.

Q. Would you agree that interobserver variability is greater when a tumor is poorly differentiated?

A. Yes.

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Q. Would you also agree that interobserver agreement regarding subtyping of adenocarcinomas is poor?

A. I would agree with that in general; but I think, if you would take a group of people that all agreed on the criterion before they looked at it, it would actually be very good. I think that's the problem, that pathologists have their own ideas of what a tumor should be classified, but they don't frequently take the time to look up the rules.

Q. Do you think that study, then, that eliminated interobserver variability in terms of diagnosing some types of adenocarcinoma -- let me rephrase the question.

If you had a study that was done on a particular subtype of adenocarcinoma and the same pathologist reviewed all the slides, would that eliminate the problem you're talking about with interobserver variability?

A. That would eliminate it by definition. Whether or not that pathologist would be right would be another question, but it would be eliminated.

Q. If he was right, he would be right all the time; and if he was wrong, he'd be wrong all the time?

A. That's right.

Q. What is tumor heterogeneity?

A. That's what I think is very common in tumors. It's that you can see one pattern of a cancer in some areas

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and other patterns in another area. When you look at it through a microscope, part of a tumor can look a certain way and another part of the tumor can look another way. That's, I would say, is present in the majority of all cancers, not only lung cancer.

Q. Is that true in your own personal experience?

A. Yes.

Q. Are you familiar with Dr. Roggli's study regarding the extent that those tumors are heterogeneous?

A. I am. And I cite that in this book.

Q. Is this true that poorly differentiated tumors are more hetergeneous than more differentiated tumors?

A. I think by definition that would be the case, yes.

Q. What is it that causes tumor heterogeneity?

A. Probably individual genetic mutations themselves, and it kind of tells the cell to do one thing and the cell is going to do another thing.

Q. Is that dedifferentiation?

A. I think of it more as differentiation. It's not really dedifferentiation. It's just that those cells -- their DNA is telling them to do another thing.

Dedifferentiation means differentiating towards another way. For example, certain cells in cancers start to produce angiogenic factors or they produce substances that break

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down blood vessel walls so they can get into the vessel and metastasize. I don't look at that as dedifferentiation. I think of that as differentiation to do a specific type of function. A way to look at it from the tumor's perspective is it allows the tumor to progress and survive.

Q. Is there a relationship between tumor heterogeneity and dedifferentiating?

A. I'm not sure, again, what you mean by dedifferentiation, but there is a relationship between tumor heterogeneity and metastasis and that prognosis.

Q. When you use the term dedifferentiation, what do you mean?

A. I don't use that term anymore. I've completely eliminated that. I'm not trying to be sarcastic or wise with you. I just think that with what we know now with respect to cancer that that's not the proper use. I think it's differentiation along the different lines that produces this heterogeneity, and how that differentiation occurs from a genetic point of view and how it's manifested morphologically is something that's very difficult to do.

Q. In the letter that you sent to Mr. Patrick, you used the term "degenerating squamous cell tumor." What did you mean by the word "degenerating"?

A. I thought a lot of the cancer cells were dying. There was a lot of swollen cells, and you can see

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that in some of these pictures here. They really were dying.

Q. Have you talked to anyone from the Ness, Motley firm about the degree of tar exposure Mr. Little consumed from Carlton cigarettes?

A. No.

Q. Have you talked with or received any information from anyone from Ness, Motley about whether or not Mr. Little blocked vent holes on the Carlton cigarettes that he smoked?

A. No.

Q. Do you know the degree to which vent hole blocking increases tar delivery to smokers who smoke cigarettes with air insulation filters?

A. No.

Q. I want you to assume that Mr. Little smoked Winston cigarettes for 15 years and Carlton cigarettes for about 20 years, okay?

A. Okay.

Q. And I want you to assume that half of the tar delivery Mr. Little received from the Carlton cigarettes was due to the fact that he blocked the vent holes on filters, and half the tar he received from Carlton cigarettes was due to his smoking the cigarettes the way they were designed to be used, okay?

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A. Yes.

Q. First of all, do you have any reason to disagree with my assumption that half the tar delivery from the Carltons was due to the vent blocking and half was due to his smoking of the cigarette the way it was designed?

A. I don't have any reason to dispute you. I don't think anything about that.

Q. Well, if that's the case, half was due to vent hole blocking and half was due to smoking the cigarettes the way they were designed, then is it your opinion, Doctor, that both halves of the tar in the smoke he received were substantially contributing causes to his lung cancer?

A. Yes.

Q. Dr. Roggli total us in his deposition that if Mr. Little had not blocked the vent holes it was more probable than not that he would not have gotten lung cancer. Do you have any reason to disagree with Dr. Roggli?

A. No. I don't think Dr. Roggli -- I guess I would say not. First of all, I don't have any reason to disagree with him. I guess that statement assumes that he would not have developed cancer because he would not have received a dose of carcinogen to cause the mutations that led to it.

Q. You don't disagree with it, right?

A. I don't disagree with it, but I guess --

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Q. My next question is: Do you agree with it?

A. I don't know if I agree with it or not. I've never thought of something that way because I guess that's assuming that you know how much carcinogen it takes to cause cancer. To me that's something that is so variable in every situation I have ever seen -- I'll use asbestos which I know a lot about -- some people develop a cancer caused by asbestos at a very low dose and other people will get phenomenal exposure to asbestos and never develop cancer.

The question is: Why is that the case? Suppose it has to do with genetic susceptibility and let's say it has to do with something like people that have high concentrations of this enzyme glutathione-s-transferase. Those people can detoxify the carcinogens better than the people that don't have that.

Say that you have a person who doesn't have any genetically-inherited glutathione and that person is exposed to carcinogens, say, where the air vents were not blocked. How you do you know that that person is not going to get a cancer at that level? That's why I don't know if I could make that same conclusion as Dr. Roggli because I think that in all carcinogen-caused cancers there's a wide range at which people develop cancer from that carcinogen.

Q. Just so I understand your view about this, you don't disagree with Dr. Roggli, and you don't agree with

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him. Basically, you are taking the view -- let me rephrase the question.

Do you have an opinion one way or the other, to a reasonable degree of medical certainty, whether or not Mr. Little would have avoided his lung cancer if he had not blocked the vent holes on Carlton cigarettes?

A. I do not have an opinion.

Q. Doctor, do you know the relative risk for developing BAC through smoking?

A. I don't know that. I don't think I've ever seen any studies where relative risk has been given for that specific subtype of adenocarcinoma.

Q. Are you aware of any peer review study, Doctor, that has shown the causal relationship between BAC and cigarette smoking?

A. I can't answer that as I sit here. I would have to look through the articles I have of BAC to see if I had something that showed an increase.

Q. Nothing comes to mind?

A. Not that I can give you a citation for, no.

Q. You said you had a collection of materials on BAC?

A. A big file on BAC, yes.

Q. How big a file?

A. Oh, probably an inch or an inch and a half.

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Q. How is that file put together?

A. From myself collecting articles over the years.

Q. In any systematic way? Tell me how you went about putting it together.

A. Most of them have to do with pathology. I've been extremely interested in BAC primarily because the nonmucinous type has a type of cell in it called Langerhans cells. I've written about that and published articles on it and have been very interested because of my interest in Langerhans cells and also my interest in the fact that there's a type of lung disease called Langerhans cell granulomatosis that's caused by cigarette smoke that's probably not cancerous, at least in most people, and it turns out that most of these BACs of the nonmucinous type have those cells in them.

Q. So if I understand you correctly, there may or may not be studies in your BAC file that report on whether BAC is associated with smoking?

A. There may or may not be. All I can tell you is the ones that have the Langerhans cells in them, as far as I know, are smokers.

That has not been the primary focus of my interest as a pathologist to see if there's an association between BACs and cigarette smoke. I've looked at it more from a

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different perspective; but I probably have some articles that talk about that, and that's why I would say that I'd have to go back and look through the files.

Q. And you certainly have not done any studies yourself to determine whether or not BAC is associated with smoking?

A. I have not.

Q. And you've certainly not made a comprehensive review of the literature?

A. I have not.

Q. You said that there were precursor lesions for BAC?

A. I believe there are, yes.

Q. I think you made the statement that there are studies showing that the lesions are associated with smoking?

A. There are.

Q. Do you have copies of those studies?

A. I can refer you to -- I don't have copies of those right here. I do have copies in my files, and I can refer you to a chapter in a book edited by Bryan Corrin. The title of the book is called Lung Cancer, and I think it's Chapter 6 or Chapter 7, written by Dr. Kerr.

It talks about atypical adenomatous or hyperplasia of the lung. That's what was thought to be the precursor

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lesion, at this point in time, of BACs.

Q. Other than that book, are you able to refer me to any other studies showing that these lesions that you identified as precursor lesions of BAC are associated with smoking?

A. There are two citations in there talking about the fact. There's two studies, and all of the cases occurred in cigarette smokers. They list the articles. In that chapter you can find that. This also lists the articles where not all of them are smokers.

Q. So all the studies that you are aware of they have in this book?

A. I don't know if all of them are but the majority of the studies are in there, yes. Most of them, I think, that I would have in my own files would be referenced in that chapter.

Q. Doctor, would you agree that in order to determine whether an individual case of BAC is associated with smoking or not that it would be necessary to rely on published studies that use the same criteria to classify BAC as were used to diagnose BAC in the individual patient?

A. I would agree with that concept in general, yes.

Q. Would that be an appropriate way, Doctor, in your opinion, in order to determine whether an individual's

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BAC was associated with smoking or not?

A. I think it would. I basically think that you're saying you compare apples with apples and oranges with oranges.

Q. If you knew the pathologic criteria that was utilized in a particular study doctrine and if the same criteria was utilized to diagnose the individual patient, then you could use that study to determine whether or not the tumor is of the type under study or isn't associated with smoking; is that fair to say?

A. I would say that would be fair to say as long as that was done accurately.

Q. As long as the criteria were applied accurately?

A. Yes.

Q. That criteria for BAC, as set forth in WHO-III, is that different than the criteria in WHO-II?

A. They are.

Q. Would you agree that the adoption of new criteria for BAC in WHO-III doesn't necessarily negate the validity of epidemiologic studies done applying the criteria for BAC in WHO-II in terms of assessing the cause of BAC diagnosed in accordance with WHO-II?

A. I would agree with that in general as long as those criteria were accurately enough applied. What is

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often done -- I guess you would have to look at each individual study on BACs, and you'd have to determine if the person who is doing the epidemiologic study was using the diagnosis from pathology reports, or did they have a pathologist who was knowledgeable in lung cancer go back and look at every one of those cases from a pathology point of view.

Most epidemiologic studies when they talk about, for example, lung cancer, they often don't subtype them. Mesothelioma is another good example. They often frequently subtype them. It would depend if they just used the diagnosis BAC off the pathology report versus going back and looking at it or if they used the diagnosis of adenocarcinoma, probable BAC type or something like. You would have to look to make sure you are comparing apples with apples and oranges with oranges.

Q. If you had a pathologist that applied the WHO-II criteria for BAC and then applied the study based on those same criteria, that would be an appropriate way, in your opinion, in order to determine whether or not that lung cancer is associated with smoking?

A. I would agree.

Q. Mr. Murphy, too, asked you some questions about the decline in relative risk that occurs when smokers stop smoking, correct?

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A. Yes.

Q. And you referred to a chart that appears on page 6 of the Short book Pulmonary Pathology of Tumors, right?

A. I did.

Q. That's figure 1.2?

A. Yes.

Q. As I understand this chart, Doctor, the mortality ratio for smokers who have stopped smoking for one to four years is roughly nineteen times that of nonsmokers, correct?

A. Correct.

Q. And for smokers who have stopped smoking for 20 or more years the mortality ratio is 2.1, correct?

A. Correct.

Q. So the decrease that occurs between the time somebody stops smoking for one to four years and the time they stop their smoking for 20 years has dropped from approximately 19 to approximately 2.1 in terms of the mortality ratio, correct?

A. Correct.

Q. That's a decrease of approximately 90 percent; is that fair to say?

A. Yes.

Q. In terms of actual observations in the

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epidemiologic studies, Doctor, does that mean that -- I just want to make sure I understand this -- that means that if we took people who had stopped smoking from one to four years -- let me rephrase the question.

Does this mean, Doctor, that for people who stopped smoking for 20 or more years and that 90 percent of them, approximately, will avoid lung cancer?

A. Yes.

Q. So if we took a group of 100 smokers who were all destined to get lung cancer if they continued to smoke and then they stopped, we would have a situation where now instead of 100 getting lung cancer that you would have 10 get lung cancer and 90 would avoid getting lung cancer, correct?

A. I don't know if you can totally make that assumption though because that's saying that everybody who smokes is going to get lung cancer, and that's not true at all.

Q. I was making the assumption that if we took 100 -- if we had way of identifying the people who were --

A. Okay. Yes, that would be correct.

Q. So if we take 100 people who are going to get lung cancer if they keep smoking and now they stop, after 20 years 90 will avoid lung cancer and only 10 will get lung cancer; is that correct?

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A. I don't know. I would have to look into that again to see if this takes all smokers because if it takes all smokers you could say that only one out of four are going to get lung cancer no matter how much they smoke. This mortality ratio says it's 20 percent of people who smoke are going to die from lung cancer, and it's actually higher than that right now. But just say 20 percent of the people who smoke are going to die from lung cancer, and then if you stop that -- no, I think it would be what you said.

Q. Just so we are on the same wave length, the observation from the epidemiologic studies is that, if you take a population that stops smoking, 90 percent of the people who would have gotten lung cancer --

A. Would not get it.

Q. -- and only 10 percent do?

A. Right.

Q. I want you to assume, Doctor, that Mr. Little stopped smoking cigarettes, and he had stopped smoking cigarettes from 1969.

Would it be fair to say, Doctor, that he would have avoided at least 90 percent of his risk of lung cancer if he had stopped?

A. Yes.

Q. Would it be fair to say that it's more likely than not that he would be one of the 90 people we were

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talking about before who would have avoided their injuries than the 10 who did get lung cancer?

A. I would agree with that, yes. More likely than not, yes.

Q. Would you agree, Doctor, that it is more likely than not that if Mr. Little had stopped smoking in 1969 that he would not have gotten lung cancer in 1995?

A. More likely than not, yes.

Q. To a reasonable degree of medical probability?

A. Yes.

Q. You told us that Mr. Little's tumor was first in existence eight years before 1995?

A. That's based on those assumptions that I made which are not totally true assumptions. That's based on a review of linear growth and what those cells die and that the tumor grows at the exact same rate.

Q. Do you have an opinion to a reasonable degree of medical certainty as to when Mr. Little's tumor first came into existence?

A. That, again, is --

Q. Let me rephrase the question.

A. Okay.

Q. Do have an opinion to a reasonable degree of medical certainty as to when Mr. Little's tumor first started to develop?

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A. If I understand the question, it's one of the first cancer cells developed. All I would say is that if you go by the calculation that we did it would have been approximately 1987.

Q. Is that when all the steps that were necessary to the development of his cancer were completed?

A. If you assume that these calculations are right. The thing you have to remember in all of these is that there's always a range in the doubling time. There is no way that I can tell -- although, there actually is in this case maybe a way that you could tell.

If you assume that that 1993 x-ray report that said that the tumor was 1.5 centimeters in diameter, and if you took the next x-ray report and you said it got to 4.2 -- you'd have to calculate what it was on the x-ray and make sure that those x-rays are very similar as far as the technique used and if the patient was the same distance from the x-ray machine, et cetera, et cetera.

You could actually calculate what the doubling time was because that's how it was initially done. You use the volume of the sphere and you use the increment in days and then you make some other assumptions, and you could do that. In fact, I think there's a little nomogram in this book that let's you do that.

Q. Then you would just extrapolate backwards in

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terms of how many doublings there are?

A. Right. Then you could make a graph and if you knew the doubling time and made those assumptions, you could actually calculate back.

Q. But you haven't done that?

A. I have not done that because I didn't know until today that there was a possible observation of a tumor back in 1993.

Q. As you sit here today, is it your best estimate that this tumor first arose as a complete tumor in 1987 or 1988?

A. Again, that's just a standard doubling time calculation and making the assumptions I made. Can I say how accurate it is? No. I can't say that it's very accurate. That's just a standard calculation.

Q. Do you know how many steps were involved in the development of this cancer?

A. No. I think that from what these review articles say there has to be at least -- I think every solid tumor that's been examined -- I'd have to check this -- has undergone at least two mutations and tumor-suppressor genes, and I can't remember how many mutations in proto-oncogenes.

Q. Do you know how many mutations of tumor-suppressor genes or proto-oncogenes were involved in Mr. Little's tumor?

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A. No. There's no way to do that unless you go back and test it. I think you probably could do that today if somebody wanted to do that by PCR.

Q. You have not done that?

A. I have not done that. Maybe Dr. Barsky has done that. I've not done that.

Q. Are you able to, Doctor?

A. Not this, just a -- I'm not going to do that although I'm very interested in it.

Q. Is it something you wouldn't do yourself?

A. I'd love to do that. If I was 20 years younger, I might be in that field of medicine.

Q. But you're not in that field now?

A. I'm not in that field, and I'm too damn old to go back.

Q. Doctor, can you identify any of the specific genetic events that led to Mr. Little's cancer?

A. I can not, no.

Q. And can you identify the role that smoking played in any of those steps?

A. I can't identify the specific role. All I know is that there is this very strong association between lung cancer and cigarette smoking, and that's what I've observed myself and that's what has been published in the literature.

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I think, basically, at this point in time, about 90 percent of all common lung cancers are caused by cigarettes.

Q. But as you sit here today you are unable to tell us which specific events were involved in Mr. Little's cancer and the role that smoking may or may not have played in any of those specific events?

A. That would be true, and I think you can say that for basically every lung cancer unless somebody went back and specifically looked, and somebody could go back and specifically look. If they wanted they could look for various tumor-suppressor gene mutations.

Q. Doctor, up until the time that all of the genetic events that were necessary to cause this cancer, is it possible that Mr. Little could have avoided his cancer by stopping smoking?

A. I think that is possible, yes.

Q. Are you able to attach a probability to it?

A. Well, all I can say is that we know that if it got to the point of even -- certainly in cervical carcinoma of the female uterus, there have been cases where carcinoma in situ has not progressed into invasive carcinoma. There also have been cases where carcinoma in situ in the bronchus has been identified where at least for the observed time the tumor has not progressed to an invasive carcinoma. I don't know if that time period was long enough to totally exclude

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that it didn't invade.

Q. As far as you are aware, carcinoma in situ does not inevitably give rise to invasive carcinoma?

A. At least theoretically it doesn't, but yet I think that it's a stage that all solid tumors go through is carcinoma in situ. It doesn't inevitably, at least in certain systems that we have studied.

Q. Even at that point it's possible that a smoker could avoid cancer by smoking cessation?

A. I would say it's possible. I don't know. I don't think I could give you any a number of what -- say, if you had 100 people that had carcinoma in situ of, say, the bronchus or, say, 100 people with adenomatous hyperplasia of the lung, how many of those would progress and how many of those would not progress if they stopped smoking.

Q. Other than to say it's possible you are unable to attach a probability to it; is that fair to say?

A. I am unable to attach a probability. That's fair to say.

Q. Now, one of the things you said was that the etiology of all carcinomas with the exception of small cell carcinoma is to some extent uncertain?

A. I don't think I quite said that. I tried to say that if you look at lung cancers and cigarette smoking, the one that is the most strongly associated is small cell

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carcinoma. The next most common would be squamous carcinoma. The one that would be the least commonly associated is adenocarcinoma and large cell undifferentiated carcinomas.

I think I also said that in my own experience that the majority of that type of tumor that I have seen where I work in Bremerton, where I worked at Virginia Mason, what I saw in the lung cancer studies group occurred to people that were smokers. I would say that in the lung cancer study group, where we looked at that in the pathology section, is that 90 percent of the adenocarcinomas in all people were smokers.

Q. Would you agree, Doctor, that the same thing that causes lung cancer in nonsmokers also causes lung cancer in smokers?

A. Could you say that again?

Q. The same things that cause lung cancer in smokers -- I'm sorry. Let me say it again.

Would you agree that the same things that cause lung cancer in nonsmokers also cause cancer in smokers?

A. From a theoretical point of view the answer is yes.

Q. There is no reason to think that smoking protects people from other causes of cancer, is there?

A. There would be no reason that I know of to

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suspect that, no.

MR. RILEY: Subject to the comments made earlier in the deposition by Mr. Murphy and myself, I have no further questions at this time.

(Ending time: 5:10 p.m.)

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REPORTER'S CERTIFICATE

STATE OF WASHINGTON)
) ss
COUNTY OF PIERCE)

I, SUELLEN H. SHAW, CSR No. SHAW*SH565PS, Certified Court Reporter, certify;

That the foregoing proceedings were taken before me at the time and place therein set forth, at which time the witness was put under oath by me;

That the testimony of the witness, the questions propounded, and all objections and statements made at the time of the examination were recorded stenographically by me and were thereafter transcribed;

That the foregoing is a true and correct transcript of my stenographic notes so taken.

I further certify that I am not a relative or employee of any attorney of the parties, nor financially interested in the action.

IN WITNESS WHEREOF, I have hereunto set my hand and affixed my official seal this 10th day of April 2000.

SUELLEN H. SHAW
CCR No. SHAW*SH565PS
Notary Public in and for the
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REPORTER'S CERTIFICATION OF CERTIFIED COPY

I, SUELLEN H. SHAW, CCR No. SHAW*SH565PS, a Certified Shorthand Reporter in the State of Washington, certify that the foregoing pages 1 through 242 constitute a true and correct copy of the original deposition of SAMUEL P. HAMMAR, M.D., taken on April 10, 2000.

I declare under penalty of perjury under the laws of the State of Washington that the foregoing is true and correct.

Dated the 13th day of April 2000.

SUELLEN H. SHAW, CCR No. SHAW*SH565PS

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